

A HANDBOOK ON DIABETES MELLITUS AND ITS MODERN TREATMENT

By

J P BOSE, M.D. (C.S.), F.C.S. (Lond.)

IN CHARGE DIABETES RESEARCH CALCUTTA SCHOOL OF TROPICAL
MEDICINE PHYSICIAN IN CHARGE OF DIABETES DEPARTMENT,
CARMICHAEL HOSPITAL FOR TROPICAL DISEASES CALCUTTA

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Thoroughly revised partly re-written and brought up to date
ILLUSTRATED

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To
MY PARENTS

PREFACE TO THE FOURTH EDITION

This volume gives in brief facts and figures which I have gathered during the last 28 years i.e. since I had initiated and organised in 1922 a new department in the School of Tropical Medicine for research and investigation in diabetes with particular reference to its special problems relating to India where diabetes is extremely common and the mortality particularly among the rich and the intellectual classes very high.

As in the previous editions my aim has been to bring the most up-to-date useful and practical information regarding the disease before the busy practitioner and the medical students. Endeavour has been made to present the whole subject to the reader in a systematic and practical manner giving particular attention to facts affecting Indian conditions and Indian ways of life. This specially applies to the Diet section which has been completely overhauled, enlarged and partly rewritten. The author's system of dieting has also been remodelled and new scales of dieting suitable for vegetarians and non-vegetarians both Indian and European have been incorporated. The food tables in the book have been brought up-to-date involving much thought and labour.

The book has been thoroughly revised and rearranged and in view of the new work done within recent years many of the old data have given place to new ones. This has meant substantial changes in some of the chapters and some of them had to be entirely rewritten.

Emphasis is once more laid upon the opinion held by the author that with the advance in the knowledge and the treatment of the disease there is no reason why the diabetics of to-day should not live as long or as comfortably as their fellow non-diabetics provided they are honest and willing to carry out the treatment faithfully.

Since the discovery of Insulin it may be said that at least four outstanding achievements stand out in bold relief viz—(1) lengthening of diabetic lives and their increased efficiency (2) the ease and safety with which surgical operations can be performed (3) the possibility and safety of pregnancy in diabetic women and (4) the practical elimination of diabetic coma

If the present edition of the book proves as useful and successful as its predecessors in achieving the aim and object of the author namely to spread the most recent knowledge of the disease among all those concerned the author will consider his labours amply recompensed

J P B

The Sanctuaries
41 41, Bagh Bazar Street
Calcutta April 1949

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CHAPTER I

HISTORY AND PROGRESSIVE KNOWLEDGE OF THE DISEASE

THE history of diabetes can be traced back to the time of Moses. In Papyrus Ebers an old Egyptian medical compilation there is mention of a disease called polyuria which in all respects appears to resemble diabetes closely.

Among the ancient Greek writers the first mention of this disease is to be found in the writings of Aretaeus of Cappadocia (Circa, A.D. 150). This eminent physician is believed to have been a contemporary of Galen and in the description of the disease he lays particular stress on polyuria and thirst. The important point that the urine of diabetics contains sugar appears to have escaped the notice of all early European writers. But if we refer to the old Hindu medical literature we find that this important clinical factor is mentioned in the Charaka Samhita a compendium made by the renowned Hindu physician Charaka (2nd century A.D.). It appears that Charaka collected his materials from a much earlier work of Agniveya, who again based his writings upon the teachings of his master Atreya (6th century B.C.). Susruta (A.D. 500) gave a recognizable description of diabetes mellitus as *Madhu Meha* (or *Ikhu Meha*) or Honey urine and described the symptoms of thirst, foul breath, voracious appetite and lingour.

Among the European writers Thomas Willis an English physician of repute first noted the characteristic sweet taste of diabetic urine in 1670 thus establishing the basic principle for diagnosis between Diabetes Mellitus (diabetes with sweet urine) and Diabetes Insipidus the insipid form (with insipid urine). The real cause for this sweetness however was not recognized till a century after

wards (1776) when another English physician Matthew Dobson of Liverpool demonstrated the presence of sugar in diabetic urine by fermentation and other tests.

The first hint that the pancreas is necessary for the complete utilization of carbohydrate food in animals dates as far back as 1682. In that year Johann Conrad Brunner of Switzerland excised the pancreas of a dog and found that the animal developed extreme thirst, hunger and polyuria. Brunner's experiment appears to be a pioneer one from the point of view of the internal secretion therapy though the exact significance of the very important results obtained was not at all recognized by the author himself. Brunner (who may be remembered as having discovered Brunner's glands in the duodenum) with his friend Peyer (who helped him in the experiment and incidentally discovered lymph nodes in the intestinal mucosa) thought that the intestinal digestion was carried out by Brunner's glands and Peyer's patches and that the pancreas was of no importance. The result was that for more than a century and a half no one thought it worth while to work on this line.

The greatest advance from the point of view of research work on diabetes may be said to date back to the time of Claude Bernard (1813-78) a pupil of Francois Magendie (1783-1855) the pioneer of Experimental Physiology in France. Our knowledge of the functions of the liver and the pancreas will always be associated with the great name of Claude Bernard. This eminent physiologist had an inherently wonderful power of thinking physiologically. Claude Bernard's attitude towards scientific investigation is best summed up in his own words which should be the proper attitude of every scientific worker. Put off your imagination as you take off your overcoat when you enter the laboratory but put it on again as you do your overcoat when you leave the laboratory. Before the experiment and between the whistles let your imagination wrap you round, put it right away from you during the experiment lest it hinders your observing power.

Claude Bernard's famous discovery of the glycogenic function of the liver was arrived at somewhat accidentally by the finding of sugar in the hepatic vein of a dog fed on sugar. A large number of ingenious experiments had to be undertaken before Claude Bernard finally established the glycogenic function of the liver on a permanent basis and succeeded in isolating glycogen.

In 1810 Bernard made his most celebrated discovery that a puncture (pique) of the floor of the fourth ventricle of the brain in dogs produces temporary glycosuria. In 1836 he proceeded to study the effect of the extirpation of the pancreas in order to see whether diabetic symptoms would thereby be produced. His experiments however did not produce the desired result probably because the extirpation was not complete.

Following Claude Bernard several other workers tried the same process but they did not come to any definite conclusion and it was left to Minkowski and Von Mering to make a memorable discovery which in fact may be considered as the foundation on which the work of subsequent investigators was built. In 1889 they succeeded in producing acute and fatal diabetes in animals by complete extirpation of the pancreas.

Long before the famous discovery of Minkowski and Von Mering Paul Langerhans (1869) an anatomist had described a peculiar group of cells in the pancreas which had since been known as the islands of Langerhans. Kuhne and Lea a few years later showed that this group of cells received a very regular and abundant supply of blood. In 1893 Laguessac and Diamare showed that the islet cells of the pancreas were distinct and separate from the secreting cells and occurred in the pancreas of all vertebrates. In 1895 Sir F. Sharpey Schafer suggested that diabetes might be caused through pathological changes in the islet cells of the pancreas. It was Lepine however who definitely formulated the hypothesis that there was an internal secretion in

these islet cells which controlled the carbohydrate metabolism. This was also suggested by Minkowski.

Reference should also be made to the works of Lepine and Hedon in France and Hale White Rennie and Fraser in Great Britain all of whom prepared alcoholic extracts of the pancreas by different methods and administered them to diabetic animals but their researches in this direction did not meet with sufficient success to justify the administration of the pancreatic extract in the treatment of diabetes. Zuelzer a German investigator was somewhat more successful in this line. In 1908 he prepared an alcoholic extract of the pressed out juice of adult ox pancreas which when injected subcutaneously into animals removed the hyperglycemia and glycosuria produced by the administration of adrenalin. Encouraged by his success in animal experiments Zuelzer tried this extract on eight diabetic patients and in five of them decidedly favourable results were obtained. The glycosuria became less, acidosis decreased and the general condition of the patients improved and great hopes were entertained in 1908 that an anti-diabetic hormone had at last been discovered. Unfortunately however the extract prepared in this crude way gave rise to very marked toxic symptoms which overshadowed the beneficial action of the extract in such a way that further treatment by this method had to be given up. This must be recognized as a brilliant piece of research work well begun and given up in haste and Zuelzer is entitled to credit for very nearly isolating insulin about twelve years before its actual discovery.

In Great Britain Rennie and Fraser continued to work independently on these lines but the extracts prepared by them from the pancreas did not produce much beneficial effect on diabetic symptoms when given by the mouth. In one case they tried the extract by subcutaneous injection but though there was definite improvement in the general condition of the patient the toxic reactions were so marked that further attempt had to be given up. Like Zuelzer of

Germany they worked their way very near to the discovery of the elusive hormone but the repeated failures discouraged them from making any further attempts in the same direction.

In 1909 McCallum ligated the pancreatic duct in a dog draining the tail third of the pancreas. No glycosuria followed. Seven months afterwards he excised the remaining two-thirds of the pancreas. This was followed by mild glycosuria. Three weeks later he removed the tail third which had begun to degenerate by that time due no doubt to the previous ligation of the duct. This second operation resulted in severe and fatal diabetes.

In 1912 Kirkbridge repeated McCallum's experiment and corroborated his results. He definitely proved that the atrophied tissues resulting from the ligation of the pancreatic duct contained healthy islet tissues and it was only the acinous tissues of the pancreas which went to degeneration.

In the same year Knowlton and Stirling published the results of their experiments which showed that the power of utilizing sugar by a diabetic heart outside the body was markedly decreased in comparison with that of a normal heart under similar conditions. Their conclusion was that in diabetes the tissues are unable to utilize carbohydrates properly. By adding extract of pancreas in weak acid to the perfusion fluid they showed that the utilization of sugar by the diabetic heart could by that process be made to approach normal.

Various investigators worked independently on this subject of preparing an active anti-diabetic hormone free from toxic effects but the full credit for first publishing a practical method of preparation of insulin belongs to Dr F. G. Banting of Toronto. A young orthopedic surgeon Banting had a great love and zeal for research work. In November 1920 he conceived the idea of preparing an active extract from the atrophied pancreas brought about by the ligation of the pancreatic duct. He argued that the

extract from the whole pancreas as used by other workers before him (without much success) must have contained proteolytic enzymes which had a destructive action on the hormone. He thought that if he tied the pancreatic duct of a dog the entire pancreas would atrophy but the islands of Langerhans would be left intact. He then proceeded to perform this experiment in collaboration with his friend Mr C H Best (who was only a second year medical student at the time) their efforts were crowned with great success and on July 27th 1921 a memorable day in the annals of research they had the satisfaction of finding that the extract which they had prepared from the atrophied pancreas (brought about by the ligation of the pancreatic duct) when injected subcutaneously or intravenously in diabetic dogs reduced both hyperglycaemia and glycosuria. Thus 32 years after the epoch making discovery of Von Mering and Minkowski another similar discovery was made in the field of diabetes by Banting and Best. The work was performed in the laboratory of Prof Macleod of Toronto who with the assistance of Prof Collip was of immense help in the subsequent preparation and the refining of the active principle to which the name Insulin was given.

Permanent and world wide recognition of this great accomplishment in Medicine has been given by the award in 1922 of the Nobel Prize to Professors Macleod and Banting who with the finest spirit of fairness and professional generosity divided the award between themselves and their co workers Drs Best and Collip.

CHAPTER I

INSULIN AND ITS LATER MODIFICATION

Insulin is essential to the functioning and maintenance of life. All of us need insulin, the requisite amount of which is manufactured and regulated in our own system in the pancreas.

In normal healthy individuals Nature regulates the supply of insulin with almost clockwork precision according to (1) the amount of carbohydrate consumed and (2) the amount of energy expended by physical labour, thus keeping a balance between production and expenditure. The three main factors which come into play in regulating the supply of insulin are (1) amount of carbohydrate consumed (2) amount of glycogen stored and (3) depletion of the glycogen store by sudden demands made on it e.g. physical exercise etc.

The islands of Langerhans in the pancreas play an important part in the production of insulin. The weight of the pancreas in a normal healthy adult is about 66 grammes, the islands of Langerhans constituting about 3% of its total weight.

The normal human pancreas usually contains about 500 000 islets. Three types of cells are known to be present in these islets—the alpha, beta and D cells so named by Bloom in 1931. Of these the beta cells are thought to be concerned with insulin production though the evidence adduced in its support is yet inconclusive. The functions of the other two are still unknown.

The average insulin content of the normal human pancreas has been estimated at 1.7 units per gramme. The insulin content of diabetic pancreas is however very much less, sometimes coming down to 0.4 units per gramme or even lower. The total insulin production in a normal

healthy individual, with a daily intake of 400 grammes of carbohydrates and 2500 calories has been roughly calculated to be about 50 units per day

The diabetic patients of the present day however are fortunate in that they can to a great extent overcome this handicap by availing themselves of artificial supplies of insulin. This was not possible before Banting's discovery in 1921. It appears to-day that given the proper facilities there is no reason why the diabetics of the present day should not live as long as his fellow non-diabetics provided they are intelligent, honest and willing enough to carry out the treatment prescribed for them

Mode of preparation of insulin

Various modifications by different authorities have been introduced in the mode of preparation of insulin since its discovery. It is not the object of this book to go into the details of these methods. The first method employed for its preparation was the extraction of the active substance from normal ox pancreas using alcohol as a means of preventing the enzyme action a method originally employed by Scott. Dudley made further modifications by precipitating the active material with picric acid and then converting the insoluble picrate into soluble hydrochloride by means of an alcoholic solution of hydrochloric acid. This hydrochloride is a whitish powder of which 0.5 to 1 mg will lower the blood sugar of a two-kilo rabbit to about 0.01 per cent and cause typical hypoglycæmic convulsions.

The method of preparation of Insulin as given in the *British Pharmacopœia* 1932 (Seventh Addendum 1945) is summarized below —

The pancreas which must be either fresh or kept frozen from the time of removal from the body is finely sliced. Alcohol (95 per cent) is then added until the concentration of ethyl alcohol is about 60 per cent $\forall \forall$ together with a sufficient quantity of Hydrochloric Acid to make the reaction of the mixture not less than pH 3.0 and not more than pH 3.5. The mixture is then filtered and the filtrate evaporated to small bulk to which alcohol (95 per cent) is added until the concen-

tration of ethyl alcohol is between 60 and 70 per cent v/v. A precipitate of inert matter is removed by filtration. To the filtrate dehydrated alcohol is added until the concentration of ethyl alcohol is 95 per cent v/v. The precipitate so obtained is collected and dissolved in water. The active material is separated from this solution either by adjusting the reaction of the solution to the iso-electric point (which lies between the limits corresponding to the values pH 5 and pH 6) or by adding Trinitrophenol. The precipitate obtained in the former way is dried and powdered. The precipitate obtained in the latter way is dissolved in a solvent containing 6 volumes of alcohol (90 per cent) to 1 volume of dilute Hydrochloric acid and 1 volume of distilled water. This solution is poured into excess of Acetone and the resulting precipitate is dried and powdered. The necessary quantity of the dry powder is dissolved in distilled water acidified to a reaction between limits corresponding to the values pH 3 and pH 4. To the acidulated water used for dissolving the powder a sufficient proportion of some antiseptic to prevent the growth of any organism which may be accidentally introduced in the process of removing a portion of the contents of the container is added. The solution is sterilised by passage through a bacteria proof filter the potency is determined and the strength is adjusted. It is then distributed into sterilised containers in which it is sealed.

One pound of fresh beef pancreas contains on an average 2 800 to 3 100 units of insulin.

Chemistry of insulin

Crystalline Insulin in a high degree of chemical purity was first prepared by Abel and Geiling in 1926 by the Brucine Pyridine Ammonium Acetate method and the crystals are described as being doubly refractive melting sharply at 233°C.

Its empirical formula was described as $C_{25}H_{45}O_4N_{11}S + 3H_2O$. Its molecular weight was estimated to be about 35 000 and iso-electric point at pH 5.3 to 5.5. It is optically active and laevo rotatory.

According to most observers Insulin is believed to be a complex protein derivative possibly of the nature of a proteose. It gives positive Biuret, Pauly, Millon and Ninhydrin reactions. It is composed of well known amino acids namely tyrosine 12 per cent, cystine 12 per cent, glutamic acid 21 per cent, leucine 30 per cent, arginine 3

healthy individual, with a daily intake of 400 grammes of carbohydrates and 2500 calories, has been roughly calculated to be about 50 units per day

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One pound of fresh beef pancreas contains on an average 2000 to 3000 units of insulin.

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According to most observers Insulin is believed to be a complex protein derivative possibly of the nature of a proteose. It gives positive Biuret, Fehling, Millon and Ninhydrin reactions. It is composed of well known amino acids namely tyrosine 12 per cent, cystine 12 per cent, glutamic acid 21 per cent, leucine 30 per cent, arginine 3

quotient* has been found to take place under its influence. It causes the disappearance or marked reduction of the hyperglycemia as well as of the urinary sugar and the ketone bodies, thus tending to restore the diabetic individual to normal condition.

Thus we see that the total effect of a dose of insulin on blood sugar appears to depend on

- (1) the glycogen content of the liver;
- (2) the hydrogen ion concentration of the blood.

As the pH of the blood decreases, there is an augmented glycogenolysis and hence the hypoglycæmic action of insulin is neutralized to some extent. This is the reason why, in cases of diabetic acidosis, relatively large doses of insulin are required to reduce the blood sugar.

Physical exercise taken during the period of insulin activity will greatly accelerate its hypoglycæmic effect. This will be explained afterwards.

Insulin hypoglycæmia

When a patient is given too large a dose of insulin the blood sugar falls below the normal level, producing a train of symptoms within 1 to 8 hours after the patient has received the injection.

The symptoms of hypoglycæmia usually begin with a feeling of anxiety which the patient cannot account for. The patient feels as if some trouble is impending. There may be restlessness, tremulousness and even actual tremor, particularly of the extremities. This is sometimes so marked as to make fine movements (such as writing, threading a needle, etc.) impossible. One of the most noticeable symptoms manifested at this stage is a great desire for food. Dimness of vision, sometimes diplopia or double vision.

* This term is used to indicate the ratio between the amount of carbon dioxide excreted in the expired air and the amount of oxygen consumed. It is thus indicated as CO_2/O_2 . If glucose is completely oxidized into CO_2 and H_2O the respiratory quotient is 1. In diabetes the respiratory quotient is below 1 (about 0.7 or so).

may occur. A isomotor disturbance is quite common. pallor of the skin alternating with flushing may be present and there may be profuse sweating which is sometimes a very characteristic symptom. The pulse rate is sometimes markedly increased. The severity of these symptoms increases with the degree of hypoglycæmia. When the blood sugar level gets below 0.05 per cent, very acute symptoms may develop. The body temperature gets low, the blood pressure falls, the patient may get aphasic and the deep reflexes are lost. Convulsions may take place with low muttering delirium and the patient may gradually pass into a comatose state.

Causes of insulin hypoglycæmia—The various causes leading to hypoglycæmia may be summed up as follows—

- (1) Too large a dose of insulin given in one injection brings on hypoglycæmia.
- (2) Administration of insulin too long before meals may result in hypoglycæmia.
- (3) Delay in digestion or failure in the absorption of food as in vomiting, diarrhoea etc. may produce hypoglycæmic symptoms.
- (4) Hard exercise taken immediately after insulin injection may cause hypoglycæmia.
- (5) In cases of complications (e.g., infection, coma etc.) where large doses of insulin are required temporarily, it may suddenly cause too much lowering of the blood sugar if the large doses are continued even after the subsidence of the main complications for which the large doses were given.

Treatment of insulin hypoglycæmia—Fortunately all the serious symptoms of hypoglycæmia detailed above are amenable to prompt treatment. If the patient is conscious the ingestion of carbohydrate in the form of 4 to 8 oz. of orange juice or a tablespoonful of glucose relieves these symptoms within a quarter of an hour. If the milder symptoms are not detected or given heed to and they are allowed to pass on to the coma stage 10 to 15 minims of sol

adrenalin chloride (1 in 1000) given subcutaneously may gradually restore consciousness within 5 to 15 minutes. Glucose can also be given by the mouth or intravenously. A dose of pituitrin (1 cc) given subcutaneously also produces good results.

If there is collapse keep the patient warm give hot coffee per rectum and also stimulants like camphor, strychnine etc.

Standardization of insulin dosage

The *physiological unit** of insulin is that amount which on subcutaneous injection in a starved rabbit (not less than 1 kilogramme in weight) can lower the percentage of blood sugar to about 0.045 per cent within 3 to 4 hours and produce typical hypoglycæmic convulsions. The international clinical unitage however as adopted by the Health Section of the League of Nations is one third of the above strength—three *clinical units* being thus equivalent to one *physiological rabbit unit*.

The reason why 0.045 per cent was chosen as the percentage to which the sugar should become lowered in the standardization process is that at this level almost without fail the animal develops highly characteristic symptoms of hypoglycæmia consisting of violent convulsive seizures with intervals of coma. These symptoms may finally terminate in death which however can be prevented by the subcutaneous or intravenous injection of dextrose (one gramme per kilo of body weight).

Keeping properties of insulin

When insulin came to India in the latter part of 1922 there was a great deal of controversy among different workers in regard to its potency and keeping qualities. Some

* The International Standard amorphous insulin powder contains 8 units per milligramme. It is dry soluble insulin kept in the National Institute for Medical Research and the unit is the specific activity contained in 125 mg of this standard preparation.

people definitely asserted that insulin lost nearly all its potency owing to heat in the tropics. The author worked on this problem for some time and the results of his investigation definitely showed that the alleged deterioration of insulin was more apparent than real and was really due to variations in the experimental animals.*

It was found, for instance, that the albino Himalayan type of rabbits (which were generally used for the purpose of standardization of insulin out here) were very resistant to insulin action as compared to the brown Belgian hare type of rabbits (which were used in England and on the Continent for insulin standardization). In investigating the reason for the variability of insulin action in the two types of rabbits it was found by experiments that the adrenalin content of the albino Himalayan was high and as such was capable of inhibiting the action of insulin to a large extent. This subject will be further dealt with in Chapter VII.

Insulin has been found to keep fairly well if it is kept in a dry and cool place and if precautions are taken to prevent contamination during use.

* The variability in rabbits used for the assay of insulin—Bose, I. P., and Acton, H. W., *Indian Medical Gazette*, Vol. LX, No. 7, July, 1924.

Europe the disease is said to be most prevalent in France especially in Normandy

In India the disease is extremely common in Bengal specially among the rich and the educated classes. The cause appears to be a combination of ill balanced diet over eating sedentary habits excessive intellectual work and too much mental worry inseparable from the present struggle for existence. The Bengalee Hindus appear to be more prone to get diabetes than any of the other races living in India

The latest statistics collected by the author of 3 500 cases of diabetes give the following percentage of racial incidence of the disease —

	per cent
Hindus	47.3
Muslims	23.1
European (including Anglo-Indians)	24.2
Other cases	5.4

A very striking feature which becomes evident at once from the above statistics is that it appears to show a great preponderance of the disease among the Hindus as compared to the Mohammedans. As a matter of fact the incidence of the disease among the Mohammedans appears to be less even than among Europeans. This according to the author does not represent the actual state of affairs. The author is definitely of opinion that the apparent lower incidence of the disease among the Mohammedans is due in a great measure to the great reluctance on the part of the Mohammedan women to make their complaints known unless they are of such a nature as to cause much physical suffering.

Age of onset and prevalence of diabetes

A classification of
the author's

cases

CHAPTER III

INCIDENCE OF DIABETES AND MORTALITY AND SOME OF THE COMMON ETIOLOGICAL FACTORS

THE usual definition of diabetes as given in the text books is far from satisfactory. In old books we find it described as a condition of the body in which sugar appears in the urine. But there may be many conditions other than diabetes in which one may pass abnormal amounts of sugar in the urine. Diabetes mellitus again is the name indicates has been taken to mean an excessive flow of sweet urine. This we also know cannot be a proper definition as it would then include many conditions like pituitary tumours renal glycosuria etc. The urine of a normal pregnant woman is often excessive and there may be lactosuria but it certainly does not fall within the category of diabetes.

Diabetes however may be defined as a constitutional disorder due to deficiency in the secretion of the islets of Langerhans in the pancreas resulting in a disturbance of the normal utilization and storage of carbohydrates as evidenced clinically among other factors by persistent hyperglycæmia with or without glycosuria.

Racial incidence of diabetes

It has been stated by most observers that Jews are particularly liable to become diabetics. It is perhaps their rich diet and sedentary habits more than any racial tendency which are responsible for the higher incidence of diabetes among them. Diabetes is much more prevalent in America than in Europe as will appear from the mortality figures given later on. Diabetes is said to be less common among the Chinese the Japanese and the Negroes of Africa. In

large the disease is said to be most prevalent in France especially in Normandy.

In India the disease is extremely common in Bengal especially among the rich and the educated classes. The cause appears to be a combination of ill-balanced diet, over-eating, sedentary habits, excessive intellectual work and too much mental worry inseparable from the present struggle for existence. The Bengalee Hindus appear to be more prone to get diabetes than any of the other races living in India.

The following table is quoted by the author of 300 cases of diabetes give the following percentage of racial incidence of the disease:

	per cent
Europeans	4.1
British Indians	23.1
European males - aged 15-50	4
European females	5.4

A very striking feature which becomes evident at once from the above statistics is that it appears to show a great preponderance of the disease among the Hindus as compared to the Mohammedans. As a matter of fact the incidence of the disease among the Mohammedans appears to be less even than among Europeans. This according to the author does not represent the actual state of affairs. The author is decidedly of opinion that the apparent lower incidence of the disease among the Mohammedans is due in a great measure to the great reluctance on the part of the Mohammedan women to make their complaints known unless they are of such a nature as to cause much physical suffering.

Age of onset and sex incidence of diabetes

A classification of the cases of diabetes that came under the author's observation arranged according to age groupings

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The following statistics collected by the author of 5000 cases of diabetes give the following percentage of racial incidence of the disease:

	per cent
Hindus	63
Mohammedans	21
Europeans - 5000 cases for 5000	12
Other races	4

A very striking feature which becomes evident at once from the above statistics is that it appears to show a great preponderance of the disease among the Hindus as compared to the Mohammedans. As a matter of fact the incidence of the disease among the Mohammedans appears to be less even than among Europeans. This according to the author does not represent the actual state of affairs. The author is firmly of opinion that the apparent lower incidence of the disease among the Mohammedans is due in a great measure to the great reluctance on the part of the Mohammedan women to make their complaints known unless they are of such a nature as to cause much physical suffering.

Age of onset and sex incidence of " "

A classification of the cases of diabetes according to the author's observation arranged according to age and sex is as follows:

and sex gives the following percentage of incidence of the disease —

	Male	Female	Total
Children (up to 15 years)	0.35%	0.30%	0.65%
Young adolescents (16 to 25 yrs)	2.20%	1.20%	3.40%
Young adults (26 to 35 yrs)	9.40%	3.30%	12.70%
Middle aged (36 to 50 yrs)	37.60%	9.65%	47.25%
Old (51 yrs and upwards)	26.20%	9.80%	36.00%

It will be apparent from the above figures that the maximum incidence of diabetes occurs in the middle age (between 36 and 50 years) after which it declines again. Joslin who collected data from 9803 cases has shown by detailed statistics that the maximum susceptibility to the development of diabetes in males occurs at age 51 and in females at age 55. In our figures we have shown that the middle aged persons constitute 47.25% of the diabetics in India.

The percentage incidence of diabetes amongst the children and young adolescents in India however shows comparatively lower figures.

Social position and profession

Diabetes in India is extremely common among the well-to-do classes. This fact is also true to some extent in the European countries as well. According to Von Noorden the statistics of both London and Berlin show that the number of cases in the upper ten thousand exceeds that in the lower hundred thousand inhabitants.

What gout is to the nobility of England diabetes is to the aristocracy of India. The same cause i.e. chronic dietary excesses combined with indolent habits is mainly responsible for both. The difference in the nature of the diet is responsible for the presence of uric acid in the blood in one case and the excess of sugar in the other.

Among well-to-do educated Indians, specially mer-
chants, lawyers, owners of landed properties, members of
the judicial service, etc., we get evidence of some of the
causative factors of diabetes mentioned before viz. seden-
tary life, lack of physical exercise, disturbed diet over-
eating, excessive mental work.

TABLE

*Showing percentage incidence of diabetes classified
according to profession and country in 1910*

	Per cent
U.S.A. 1907	15
U.S.A. 1910	15
London 1895	1.1
London 1905	1.6
U.S.A. 1900	6.5
France 1905	6.5
France 1907	6.6
Holland 1905	6.1
Germany 1905	6.4
Germany 1907	6.6
U.S.A. 1905	6.7
U.S.A. 1910	7.0
U.S.A. 1915	7.0

Mortality

It appears from all records that diabetic mortality is
increasing all over the civilized world. Prof. Joslin published
a comprehensive statistical study of diabetic mortality in
1934 in which he stated that diabetes as a cause of death in
the United States registration area had advanced from
twenty-seventh in rank in 1900 to ninth in 1932. In England
the death rate from diabetes in 1931 was nearly 50 per cent
higher than in 1925, and 15 per cent higher than 1920.
No explanation is forthcoming of the phenomenon.

In India the state of affairs appears to be the same. The
statement of diabetic death rate in the registered area of

Calcutta and suburbs given below shows that the total death rate per 100 000 population has increased from 5.2 in 1929 to 25.9 in 1935 (the comparatively lower death rate in 1932 cannot be explained)

A partial explanation of this apparently increasing incidence of diabetes all over the world may possibly be due to the present day improved methods of diagnosis and also that both doctors and patients are more diabetes conscious now a-days

Statement showing deaths from diabetes in the registered area of Calcutta and suburbs with their rates per 100 000 population

	Total Deaths	Death rate per 100 000
1929	57	5.2
1930	89	8.2
1931	105	8.0
1932	93	7.0
1933	115	10.4
1934	210	20.7
1935	300	25.9

What then is responsible for such increasing incidence of diabetic mortality in this country? The author is of opinion that this is to a great extent due to our rapidly changing mechanized civilization which while it tends to make the people more and more comfortable and ease-loving leads to sedentary habits. The increasing consumption of sweets as well as of rich and luxury foods which appear to be inseparable from the menu of the rich and the leisured classes is another potent cause. The greater stress and strain of modern high life appears to be a third cause.

In the statement below diabetic mortality in some of the principal cities and countries of the world is given for comparison of the death rates

ÆTIOLOGY OF DIABETES

The consensus of the present day opinion is that pancreatic lesion plays the most important part in the ætiology of diabetes. Allen notes that there is a very definite relation between the severity of the disease and the amount of pancreatic tissue left in the body. He has shown by experiments on dogs that when only one tenth of the pancreas is left behind a severe type of diabetes invariably follows, with a residue of one sixth of the gland a mild type of diabetes results, with a residue of one fourth of the gland there is no spontaneous glycosuria but the carbohydrate tolerance is definitely diminished.

It will also be evident from a review of literature on the subject that the manifestation of diabetes does not depend on the loss of or damage to the ordinary pancreatic acini but the root cause of this disease centres round the islands of Langerhans though the nature of the factor or factors giving rise to the diseased condition of the islet cells has not yet been clearly understood. From the history of the literature it would also appear that the relationship between diabetes and the pancreas as also the fact that the internal secretory function of that organ has a great influence on the carbohydrate metabolism had been definitely determined by a number of observers before Von Mering and Minkowski established in 1889 the relation between the functions of the pancreas and experimental diabetes. Allen's statement in regard to this point seems to be more logical though difficult to prove. He observed that clinical diabetes arises regularly on the basis of antecedent pancreatitis and that it is now sufficiently established that the normal cause of diabetes is pancreatitis.

It has been shown by experiments that hyalinization and atrophy of the islands of Langerhans are amongst the common pancreatic changes in diabetes mellitus but the reason why the islands should undergo specific degeneration is not yet understood.

We would now consider some of the predisposing causes of diabetes which directly or indirectly throw undue strain on the islet cells of the pancreas and cause their hyaline degeneration and atrophy sooner or later.

Obesity

The association of diabetes with obesity is quite a common finding in a large proportion of cases in India. In about 50 per cent. of the cases that came under the author's observation there was definite history of the disease first appearing while the patient was in an obese condition.

The author estimated the carbohydrate tolerance in a series of cases of obese Indians, quite normal in all respects except that they were 30 to 40 per cent. over weight in relation to age and height. In about 40 per cent. of these cases he found a definite decrease of tolerance, sometimes in quite a marked degree. This in the opinion of the author may be considered to be their prediabetic stage and if these people were not careful they were likely sooner or later to become victims of diabetes.

Lawrence in his book 'Diabetic Life' goes so far as to say that to be normal or slightly under weight is an insurance against diabetes. Joslin considers diabetes to be a penalty to obesity—the greater the obesity, the more likely is Nature to enforce it. According to him the most favourable weight for longevity in middle life is 10 to 20 lb. below the average weight (calculated from the table according to the age, sex and height of the individual). Even 20 lb. below the average weight is safer than the average weight itself.

Nature of food

Excessive ingestion of carbohydrate food has been attributed by many to be a cause of diabetes in India, but, according to the opinion of the author, it does not by itself act as a contributory factor. We find that some races as

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Lawrence (1926) has definitely shown that exercise greatly increases the hypoglycæmic action of insulin. Joslin has also observed that one of his patients could do without the evening dose of insulin the day he played golf. The author holds the same view and thinks it very important that, in patients undergoing insulin treatment, the dose of insulin should be adjusted according to the exercise prescribed for him.

The following experiment carried out by the author shows the effect of exercise in augmenting the insulin action in a moderate case of diabetes. On the first day, after a preliminary blood sugar test, the patient received a dose of 12 units of insulin subcutaneously and the blood sugar was estimated every hour for the next three hours (Table A). Next day, under exactly similar conditions the patient was given the same dose of insulin but, in addition, he was made to take active exercise with Sandow's grip dumb bells immediately after the insulin injection was given (Table B). Both the results, graphically shown in the following diagram (Chart II) show the difference at a glance. It should be noted here that the patient experienced mild symptoms of hypoglycæmic shock on the second day of the experiment.

TABLE A

Effect of insulin on the blood sugar level in a case of diabetes of moderate severity

	Per cent
Blood sugar before (12 units of insulin given)	0.208
Blood sugar 1 hour after	0.163
Blood sugar 2 hours after	0.136
Blood sugar 3 hours after	0.125

TABLE B

Effect of insulin combined with exercise on the blood sugar level of the same patient

	Per cent
Blood sugar before (12 units of insulin given and exercise started)	0.210
Blood sugar 1 hour after	0.132
Blood sugar 2 hours after	0.084
Blood sugar 3 hours after*	0.063

That exercise helps in the oxidation of carbohydrates in the muscles and thus promotes carbohydrate utilization of diabetic patients seems to be undoubted at present, in

* The 1st

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Blood-sugar 3 hours after*	0.063

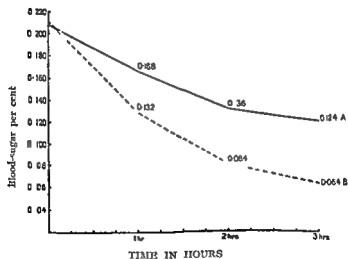
That exercise helps in the oxidation of carbohydrates in the muscles and thus promotes carbohydrate utilization of diabetic patients seems to be undoubted at present in

* The patient complained of mild hypoglycemic symptoms

view of the work done on this line. The work of Hill clearly shows that if a normal healthy individual takes physical exercise the respiratory quotient rises presumably because the carbohydrates are oxidized. Allen has stated that his diabetic dogs with known limits of carbohydrate tolerance showed marked increase in tolerance on vigorous exercise and has demonstrated this fact by blood sugar and urine tests. He has also shown that diabetic dogs which had glycosuria regularly on a daily ration of 100 gm of bread could remain perfectly sugar free with double the quantity of bread if they were regularly exercised. The author has made observations of this nature in many of his cases and is definitely of opinion that the carbohydrate tolerance of diabetic patients improves under the stress of physical exercise.

CHART II

The effect of exercise in augmenting the insulin action on the blood sugar in diabetics



(A) — Blood sugar reduction with insulin alone
 (B) — Blood sugar reduction with insulin combined with exercise

The effect of exercise appears to be even more marked in cases of diabetic children. Their improvement is found to be steadier and quicker with exercise than without it.

Strenuous exercise should, however, be avoided in severe cases of diabetes lest it induces acidosis. It has been shown that strenuous exercise in a severe case lowers the respiratory quotient, probably because it breaks down a disproportionately large quantity of fat.

One cannot too strongly emphasize the importance of the value of physical exercise in diabetes, either as a prophylactic measure or as a form of treatment in mild and moderate cases. The very pithy remark made by a Harvard professor (one of Joslin's patients), namely, that mental work makes sugar but manual work breaks it up, seems to be very appropriate. The author is definitely of opinion that lack of physical exercise is one of the most important among the ætiological factors of diabetes, especially in this country. He has come across many cases where, by suddenly giving up regular or hard physical exercise and taking to sedentary work, especially those entailing increased mental labour, diabetes mellitus was brought on. Some of these people have the erroneous impression that the excessive amount of physical exercise previously undertaken by them was the cause of their trouble and it is sometimes difficult to convince them that to go back to their old habits is their best line of treatment.

It is noteworthy that in the old Hindu medical literature, this important ætiological factor is strongly emphasized and among the causative factors of the disease are mentioned lack of exercise and laziness.

Climate

It has been stated that tropical and sub tropical climates lower the carbohydrate tolerance of individuals. Basset Smith* has stated that under the influence of the tropical

* *British Medical Journal* 31st July, 1926

here there is a tendency to retain carbonic acid in the alveolar air while the people are at rest and also a predisposition particularly in the rich to glycosuria and acidosis

Dr D. Zel Zion* working at Jerusalem Palestine has made the following interesting observations —

(1) That the sub tropical climate of Palestine in general and the hot tropical regions in particular cause a lowering of carbohydrate tolerance in the newly emigrated men and in many cases they manifest symptoms of diabetes

(2) That considerable improvement sometimes amounting to recovery results after leaving Palestine

(3) That the nature of the disease according to its response to insulin may be taken to be pancreatic diabetes

(4) That diabetes mellitus is comparatively more severe in the hot regions of Palestine than in the cooler and the mountainous regions

(5) That the course of the disease is more severe and complicated in summer than in winter

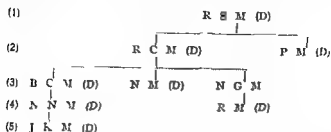
De Langen and Schut have found higher fasting blood sugar values in the white inhabitants of Java residing near the seashore but when the same individuals move to more elevated and cooler places the hyperglycemia disappeared only to reappear again when they returned to the tropical coast

Heredity

It is usually believed that diabetes is a hereditary disease. It is a curious fact in the history of most of these cases that obesity is also a hereditary factor. There are many families in which diabetes can be traced to run back for three or more generations. In one such family where both the father and the son were the author's patients and both belonged to the legal profession the disease could be traced back to the fifth generation. On account of the very

* *Arch v. fur Schiffs und Tropen Hygiene* October 1932

interesting nature of this finding the following family tree is appended (D) denotes diabetic



George Graham is of opinion that owing to family diathesis in these groups of cases the beta cells of the pancreas degenerate more readily. Begg is of opinion that heredity is an important causative factor of diabetes and so are Kellogg and many others. Dr Chunalal Bose has cited a large number of cases in support of this theory.

Joslin has also collected a large number of statistics on this head but he hesitates to attach too much importance to heredity as a factor in the onset of the disease.

The conception of the hereditary nature of diabetes appears to be an old one. A description of its hereditary character is noted in an old Indian medical literature in the seventeenth century A D.

Perhaps the true view on a consideration of these cases would be that diabetes should be looked upon as a familial affection rather than as a hereditary disease. We have no positive proof that diabetes is transmitted from parents to children. To make sure that diabetes is hereditary some of the younger members of a diabetic family should be removed from the environments and habits peculiar to the family and should be brought up amid scenes and surroundings and in ways of life which do not tend to produce the disease in a normal healthy individual. Only in those circumstances could it be ascertained whether brought up differently the child of diabetic parents shows a greater propensity to become a diabetic subject. What usually

ppens however is that children in diabetic families are made to live in the same environments and subjected to the same habits of life as the other affected members—the same family habit of suralimentation sedentary life defective hygiene and various other circumstances well known causative factors to start the disease

According to our present conception therefore a predisposition to diabetes seems to be indicated as a mendelian hereditary characteristic and this influence is now considered to be of primary importance although such predisposition may not be revealed until late in life

This naturally brings up a very important question and it is with regard to advising young diabetics about marriage. Though opinions somewhat differ on this point the author's views regarding it may be summarized as follows —

- 1 A diabetic can marry a non-diabetic with no diabetic history in his or her family
- 2 A diabetic should avoid marrying a non-diabetic who has a clear diabetic history in his or her family
- 3 A diabetic should never marry another diabetic

Age

No age is exempt but the disease is far more common among middle aged persons. The mortality from the disease however is much higher in young people than in older persons. The majority of cases which came under the author's observation were between the ages of 35 and 50 years. The youngest was an Indian boy 16 months old. This was an acute case of diabetes and he had recovered from it twice before coming to the author.

In India it has been found that a few cases suffering from infantile cirrhosis of the liver suffer from glycosuria but these should not be confused with true diabetes

Intemperance

It has been stated that alcoholism reduces the carbohydrate tolerance. However, in our experience intemperance cannot be described as a cause of diabetes in India.

Nervous origin

Excessive mental strain and emotion and constant worry have been found to bring about glycosuria and diabetes. Sudden shock to the nervous system in the shape of deaths in the family, severe loss in business etc., has certainly been found in a few cases to be the precipitating factor in causing diabetes specially of the acute type.

In 1923 the author carried out an interesting experiment which showed how nervousness and worry could bring about temporary glycosuria. He analysed the urine of some of the D. T. M. students both before and after their *in vivo* examinations and was surprised to find that 5 per cent of the students had slight but unmistakable glycosuria following the ordeal.

This temporary appearance of sugar was due probably to excitement or fright causing a marked sympathetic disturbance and the consequent outflow of an excess of adrenalin which liberated sugar from the glycogen store house of the liver, causing both hyperglycemia and glycosuria. The author while conducting certain experiments on the albino Himalayan rabbits (which are said to possess a very sensitive sympathetic system) incidentally got some very interesting results. He found that when blood was drawn quietly without disturbing the animal the blood sugar was more or less constant but when the rabbits got excited, either through fright or other causes the blood sugar shot up to about 50 per cent higher and on two occasions it became nearly double. This fact should be borne in mind by physicians securing samples of blood for sugar tests.

INCIDENCE OF DIABETES AND MORTALITY

Among other aetiological factors of direct or indirect origin may be mentioned shock of any kind especially of the head and spine brain tumours and contusions in the medulla either due to invasion by new growth or sclerosis

Insanity and glycosuria

It is stated that 10 per cent of insane persons pass sugar in their urine Henry Devine (*Recent Advances in Psychiatry* 1930) states that it is a common experience in the investigations of mental disorders to find the presence of glycosuria thus revealing a tendency in such cases to faulty carbohydrate metabolism Drury and Farran Ridge find a disturbance of sugar metabolism in each type of mental disorder investigated the most striking being observed in melancholia and confusional states In the records of inpatients of the Ranchi European Mental Hospital (communicated to the author in 1927) it was found that 7 patients out of 73 (i.e. 9.56 per cent) had glycosuria The records are too incomplete to explain this fact but they suggest interesting possibilities Out of the 7 cases of glycosuria among the female mental cases there were two cases of dementia praecox two of paranoia two of manic depression and one of secondary dementia

The present day psychiatrists hold the view that glycosuria is more often met with in the acute types of insanity than in chronic ones and that the presence of diabetes in a psychotic patient adversely affects the prognosis

Syphilis

The relation of syphilis to diabetes is not so well worked out though there has been attributed to syphilis the setting up of pancreatitis or the interference with the blood supply of the pancreas

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Insanity and glycosuria

It is stated that 10 per cent of insane persons pass sugar in their urine. Henry Devine (*Recent Advances in Psychiatry* 1930) states that it is a common experience in the investigations of mental disorders to find the presence of glycosuria thus revealing a tendency in such cases to faulty carbohydrate metabolism. Drury and Farran Ridge find a disturbance of sugar metabolism in each type of mental disorder investigated the most striking being observed in melancholia and confusional states. In the records of the in-patients of the Ranchi European Mental Hospital (communicated to the author in 1927) it was found that 7 patients out of 73 (i.e. 9.56 per cent) had glycosuria. The records are too incomplete to explain this fact but they suggest interesting possibilities. Out of the 7 cases of glycosuria among the female mental cases there were two cases of dementia præcox, two of paranoïa, two of manic depressive and one of secondary dementia.

The present day psychiatrists hold the view that glycosuria is more often met with in the acute types of insanity than in chronic ones and that the presence of diabetes in a psychotic patient adversely affects the prognosis.

Syphilis

The relation of syphilis to diabetes has not been very well worked out though there are cases in which diabetes has been attributed to syphilitic infection either by directly setting up pancreatitis or indirectly by interfering with the blood supply of the pancreas due to arteriosclerosis. How

ever, it cannot be considered as a causative factor of diabetes. Joslin states that only 16 out of his 1 000 cases (1·6 per cent) gave a positive Wassermann reaction. The author's record shows 2·5 per cent.

Infection

Severe infection of any kind may prove to be a direct cause of diabetes probably owing to some kind of damaging effect on the pancreas by the toxin. Lawrence and Buckley have shown by experiments that diphtheria toxin will practically annihilate the action of insulin. One case that came under the author's observation was that of a lad of 14 who had an acute onset of diabetes after cholera. Another, a young man of 26, had acute diabetes with grave acidosis after a severe Shiga infection.

It has been shown by Charin and Carnot that a dog may be rendered diabetic by injecting bacterial cultures into the pancreatic duct (*B. coli*, *B. pyocyaneus*, *Streptococcus* etc).

There seems to be little doubt, however, that in a diabetic patient infection of any kind definitely lowers his carbohydrate tolerance and visibly increases the severity of the disease though temporarily. The association of an infection usually of a severe nature, e.g. lobar pneumonia with the onset of acidosis and even of coma, has been noticed in a considerable number of cases.

Asphyxia

Poisoning with coal gas, carbon monoxide, carbonic acid gas, chloroform, ether, etc., has been known to bring about hyperglycæmia and even glycosuria. Mention may be made of a very interesting case of acute diabetes which came under the author's observation. The patient, a young man of 22, was a mining engineer and had at one time to work in a pit for more than 20 hours. When he came out he complained of headache and severe thirst. The

author remembers that when he came to the laboratory, he had with him an earthenware pitcher full of water and a few cocoa nuts to satisfy his thirst. He had severe polyuria and complained of a burning sensation in the whole body. His urine on analysis showed 10 per cent sugar with marked reactions of acetone and diacetic acid. His blood sugar was 0.3 per cent.

The spectroscopic analysis of his blood showed two well marked bands of carboxyhemoglobin. The patient had severe acidosis and died in coma in a few days. This was before insulin had come into use.

Trauma

Ordinary trauma cannot be considered as an ætiological factor of diabetes, but as stated before injuries to the head and spine may bring about diabetes.

Internal secretions

It has amply been demonstrated that diabetes is caused through defect in the hormone producing capacity of the pancreatic islets. Successful extirpation of the pancreas has been found to produce diabetes in experimental animals and conversely the pancreatic hormone (insulin) corrects the abnormalities in human diabetic subjects.

Modern researches have further shown that though the insufficiency of the pancreatic hormone might be the basic cause of abnormality in diabetic mellitus, there are other extra insular factor or factors influencing the causation of the diabetic state. For instance, it has been found that the pituitary gland has got a profound influence on carbohydrate metabolism. Young in 1937 produced experimental diabetes in animals by repeated injections of Ant pituitary extract. As a matter of fact, the consensus of opinion amongst the present day workers is that the anterior lobe of the pituitary gland secretes a hormone which is contra

insular i.e. it opposes insulin action and hence elevates the blood sugar level. This hormone is secreted in the cerebro-spinal fluid exerting thereby a direct action on the sugar centre of the brain stem.

It is also well known that acceleration of the internal secretions of the thyroid and the suprarenal glands may produce hyperglycæmia and glycosuria whereas defective secretions are followed by increased tolerance for carbohydrates. Glycosuria in Graves disease is a fairly common occurrence. Injections of adrenalin produce hyperglycæmia and often glycosuria and in the early state of acromegaly glycosuria is often noticed. On the other hand some cases of myxædema Addison's disease (last stage) and adiposis dolorosa show unmistakable signs of increased tolerance for carbohydrates.

*Alloxan Diabetes **

That Alloxan would induce diabetes mellitus in experimental animals was found by Jacob in 1937 who showed that the intravenous injection of Alloxan in fasting rabbits produced hyperglycæmia. Since then various workers like Bailey, McLitchie, Dunn and others worked on the same line and found that Alloxan had almost a specific degenerative action (partial or total) on the Beta cells of the islands of Langerhans.

The optimum diabetogenic dose of Alloxan varies with the animal used. With rabbits doses as small as 100 mg per kilo will usually produce diabetes.

Alloxan causes a transitory hyperglycæmia after injection in rabbits, lasting for about an hour due to excessive mobilization of glucose through stimulation of the adreno-sympathetic system followed by profound hypoglycæmia within 2 to 8 hours after injection due presumably to an over stimulation of the islet cells and finally permanent

* Alloxan is the name of mesoxalic acid having the formula $C_2N_2H_2O_4$ and is chemically closely related to purines (see ref. 1).

hyperglycæmia in 24 to 36 hours due to necrosis of the islet cells of the pancreas

Alloxan has also been found to have some damaging effect on the suprarenal cortex anterior lobe of the pituitary and the liver. The mechanism of the action of Alloxan in the production of experimental diabetes in animals has, however, not yet been clearly understood

CHAPTER IV

CARBOHYDRATE METABOLISM

So far as our present knowledge goes the outstanding feature of diabetes is a decreased capacity of the system for the utilization of carbohydrates. Normally the carbohydrates are the great energy producers of the animal organism and by reason of the ease with which they undergo combustion they supply the greater portion of the energy requirements of the body. It should be remembered that in diabetes though the sugar in the urine is chiefly derived from the non utilization of starch and sugar ingested a good portion of it may come specially in bad cases from proteins as well. Diabetes is a metabolic disorder in which the proper utilization of all the three food principles—carbohydrates, proteins and fats—does not take place. The carbohydrates in the food undergo a series of changes during the process of digestion and are eventually absorbed directly into the portal capillaries principally as glucose and in small amounts as levulose and galactose.

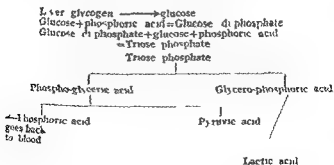
The assimilable polysaccharides (such as starch, glycogen, lactose, sucrose and maltose etc.) are all rapidly hydrolysed by the various digestive enzymes into their constituent monosaccharides which are then absorbed into the portal circulation. Unhydrolysed polysaccharides such as cellulose and pentose are not absorbed in any appreciable quantity from the alimentary canals of normal animals. The monosaccharides such as glucose are absorbed as such without hydrolysis. It was believed at one time that all sugars were converted into glucose in the course of their passage from the intestines to the portal circulation. It is known now that monosaccharides of all kinds are absorbed into the blood stream as such and are only converted into glucose after they have reached the liver.

CARBOHYDRATE METABOLISM

The portal vein thus conveys a stream of sugars to liver where, by a process of dehydration they are converted into glycogen, which is, again, whenever necessary, reconverted into dextrose for the purpose of physiological oxidation in the tissues. The liver thus serves a double function (1) as the store house for the sugar absorbed from the intestines and (2) it provides a means for the regulated reabsorption of the dextrose, helping, to a great extent, to maintain proper sugar balance in the system.

Unlike liver glycogen however the glycogen formed in the muscles (from the excess of glucose in the blood) appears to be irreversible, because once the absorbed glucose is converted into muscle glycogen, it is retained there until it is broken up (mainly into lactic acid) by muscular activities.

There is plenty of evidence in the literature of the existence of a close relationship between the carbohydrate metabolism and inorganic phosphates of the blood. It has been observed by the author,* for instance that during a stage of active carbohydrate metabolism, there is a removal of the inorganic phosphates from the blood which combine with the sugar to form a compound (hexose phosphate) which in an intermediary stage glucose is known to be finally utilized in the system. According to Meyerhof the general scheme of carbohydrate metabolism appears to follow the following path —

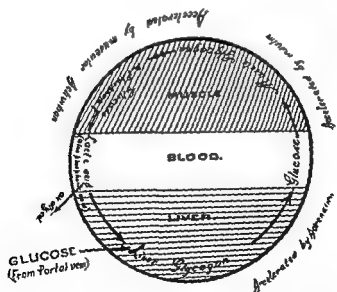


* Relation of inorganic phosphates to carbohydrate metabolism. Bone and De. *Indian Journal of Medical Research* Vol 26 January

It will thus be evident from the above that the glycogen in the muscles combines with phosphoric acid to form glucose di phosphate which undergoes a few intermediary changes before it finally breaks down into lactic acid and phosphoric acid. Part of the lactic acid thus formed (about three fourths) is carried to the liver and is rebuilt into glycogen, while the rest (the remaining one fourth) is oxidized in the system and furnishes the necessary energy. The breaking up of the muscle glycogen into the final products of lactic acid accompanies muscular activities.

Thus there exists between the liver glycogen, blood sugar and the muscle glycogen a continuous interchange governed in accordance with the resources and the physiological needs of the organism. This is shown by the diagrammatic representation given below.

Cyclic representation of the mechanism of glucose utilization in the system



Although as stated before, the muscle glycogen cannot serve as a direct source of the blood sugar (like the liver

glycogen), it may, after having been broken up into lactic acid and rebuilt into liver glycogen, help to replenish the blood sugar indirectly

Metabolism in diabetes

(1) *Carbohydrates*—The main defect in the carbohydrate metabolism in diabetes can be classified under the following two heads —

- (a) The liver loses the power of converting glucose into glycogen and storing it as such and thus the excess of the glucose, which escapes through the liver, floods the blood stream and causes hyperglycemia, when the hyperglycemia thus produced crosses the "threshold limit" glycosuria appears
- (b) The pancreas loses the power of producing the requisite quantity of insulin and hence the tissues are unable to oxidize the excess of the sugar. The result is that proper and efficient removal of the excess of sugar from the blood and the tissues does not take place and a condition of hyperglycemia and hyperglycemia persists

(2) *Protein*—A good portion of the sugar in diabetic urine is said to be derived from protein foods. We know that the protein molecules of the food are broken down into amino-acids, some of the amino acids, specially glycine, alanine, aspartic and glutamic acids etc., are *glycogenetic*, i.e., capable of producing glucose, while there are others which are *ketogenic*, i.e., tend to produce ketone bodies in suitable subjects. It is well known that in cases of severe diabetes, large amounts of sugar and ketone bodies are found in the urine on protein diet alone.

(3) *Fat*—The combustion of fats in the system is closely allied to that of carbohydrates. We know that fat needs the

fire of the burning sugar for its consumption. When fats are thus completely oxidized the final products are CO_2 and H_2O but when incompletely oxidized owing to a defective carbohydrate furnace the fat begins to smoke as it were and highly acid intermediate products such as β oxybutyric acid acetoacetic acid etc. are produced which tend to produce ketosis. It is also known that glycerol resulting from the splitting up of fats may be partly converted into glucose thus indirectly causing an increase of glycosuria in diabetes.

Influence of the nervous system and the ductless glands on sugar metabolism

Since Claude Bernard's famous discovery in 1849 viz. that the puncture of the floor of the fourth ventricle (in the space between the roots of origin of the eighth and the tenth cranial nerves) is followed by hyperglycemia and glycosuria it has been recognized that the control over the amount of sugar in the blood is in some way connected with the anatomical and physiological integrity of the nervous system. Claude Bernard's important discovery was followed by vigorous research on the subject and it was found later on that the stimulation of the great splanchnic nerve gave similar results. This led to the important inference that there was a *sugar regulating centre* in the medulla.

It is generally held that the so called diabetic or glyco-genic centre exercises its control over the liver through efferent impulses travelling along the spinal cord to the liver by the splanchnic nerves. It has also been suggested that the splanchnic nerves contain secretory fibres which control the production of the glycogenolytic ferment by the hepatic cells thus regulating the rate at which glycogen is transformed into dextrose in the liver. From the point of view of nervous control the suprarenal bodies are believed to play a prominent part in the transformation

of glycogen into sugar. The adrenals are reflexly stimulated by the great splanchnic nerves and the epinephrin thus thrown into the circulation acts on the liver cells causing a conversion of glycogen back into sugar. In support of the adrenalin theory it may be mentioned that when the adrenals are removed neither the puncture of the fourth ventricle (the so called diabetic centre) nor the stimulation of the splanchnic nerves give rise to glycosuria. We thus see why temporary glycosuria might occur during emotional states and in nervous conditions.

Increasing evidence is being obtained as to the important part which the Anterior Pituitary plays in sugar metabolism. It has definitely been shown that hyperglycemia, polyuria and glycosuria can be produced within 24 hours in healthy adult dogs by injection of extracts of the anterior lobe of the pituitary body of the ox. The mechanism of action is believed to be one of increasing glycogenolysis in the liver. It would be of interest to mention here that the work of the author in connection with glycosuria in pregnancy*, as early as 1922 brought forward interesting evidence that the pituitary played a great part in producing this condition. It has been observed that during pregnancy the anterior lobe of the pituitary shows enlargement with marked histological changes. Glucose tolerance test has been applied to a number of cases of pregnancy showing intermittent glycosuria with interesting results. The close correspondence between the curves obtained in these groups of cases and those obtained in cases of pituitary lesions with evidence of hyperpituitarism are very striking. The suggestion which the author made was that the increased activity of the pituitary body during pregnancy caused changes in carbohydrate metabolism leading to temporary glycosuria.

* Glycosuria in pregnancy—Mackenzie Wallis and J. P. Bosc *Journal of Obstetrics and Gynaecology of the British Empire* Vol. 29 No. 2 Summer 1922

It has been suggested that the anterior pituitary hormone is *contra insular* i.e. it opposes the action of insulin. The recent experiments are lending strength to the theory of the existence of a hormone in the anterior pituitary which when in excess antagonizes the action of insulin.

There are many instances in which glycosuria is associated with cerebral lesions. We know that injuries to portions of the brain in the neighbourhood of the hypophysis more particularly in the hypothalamic region produce glycosuria. Glycosuria is more frequent after injuries to the base of the skull and after cerebral hæmorrhage it is usually transitory in nature but may pass on to true diabetes. All these glycosurias resemble that produced by the puncture of the floor of the fourth ventricle.

CHAPTER V

PATHOLOGY AND MORBID ANATOMY

It has already been stated that diabetes is a disease associated with definite pathological basis in the pancreas specially in the islands of Langerhans. Cowley in 1788 was the first to observe and report the case of a diabetic with marked pancreatic damage at autopsy thus suggesting for the first time the connection between pancreatic lesion and diabetes. The importance of this discovery was however not properly recognized till a century afterwards when Minkowski and Von Mering established beyond doubt the relationship between the extirpation of pancreas and experimental diabetes.

The work of Minkowski and Von Mering stimulated further investigation on this line and as a matter of fact opened a new field of research. Minkowski also showed that if instead of removing the whole pancreas only one eighth of the gland was left behind no diabetes resulted. This partly explained the thorny question raised by some workers who had found entire absence of diabetes in individuals whose pancreas at autopsy was found to be largely destroyed either by necrosis or by malignant growths. On the other hand autopsy in many diabetic patients showing the presence of apparently healthy pancreas remained a puzzle for a long time till Opie in 1901 was able to localize the morbid changes associated with diabetes in the islands of Langerhans. Heiberg*, Weichselbaum† and Cecil as a result of investigations on a large number of diabetic cases claimed that pancreatic changes were present in almost every case and were limited to the islet cells alone in a sufficient number of cases to prove the insular theory

* Heiberg N. A. *Virchows Arch f. Path. Anat.* 1911 204 179

† Weichselbaum A. *Wien Klin. Wchnschr.* 1911 24 153

Cecil further called attention to the accumulation of evidence as regards regeneration or hypertrophy in the islands of Langerhans (34 per cent of the cases) Weichselbaum also suggested the presence of regenerative process in the islet cells—either cellular proliferation of the island epithelium or formation of new islands from the epithelium of the ducts

With the discovery of the method of differentiation of *alpha* and *beta* cells in the islands of Langerhans by Lane and the serial studies of Bensley (by his vital staining methods with pyronin) on the pancreas of guinea pigs it was hoped that there would be found some single universal diabetic lesion common to all cases; unfortunately however further study in this direction gave disappointing results

Heiberg* by counting the number of islands per 50 ccm of the gland definitely found a marked decrease in the number of the islands in the diabetic pancreas (30 to 40 instead of an average normal of 130) He was of opinion that these quantitative changes were decisive factors in the aetiology of diabetes mellitus Weichselbaum after an extensive study emphasized the importance of these quantitative changes as dominating factors in the aetiology of the disease and described the following three main types of pancreatic changes as evidenced by various changes in the islet and gland tissues

- (1) Hydrophic degeneration followed by atrophy
- (2) Chronic interstitial pancreatitis causing connective tissue proliferation in the islands with subsequent sclerosis and atrophy
- (3) Hyaline degeneration of the islands probably as a result of arteriosclerosis of the pancreatic arteries

Hyalinization of the islands of Langerhans is now considered to be the most typical pancreatic lesion in diabetes mellitus It is believed to be due to the production of an

* Pathology Kaufman Vol II p 1036

inter-cellular substance by fibroblasts when the process is sufficiently advanced a number of epithelial cells are destroyed and the islet cells undergo hyaline degeneration being practically separated from the blood supply by a more or less impermeable membrane

Morbid Anatomy

There are not many diseases in which the post mortem examination of the body furnishes us with such scanty and insufficient information as in diabetes. The author attended the post mortem of several cases of diabetes at St Bartholomew's Hospital in London and was struck with the fact that a good number of cases which during life showed undoubted symptoms of true diabetes mellitus did not reveal anything in particular at the post mortem examination except certain signs of denutrition.

(1) *External appearances*—There is usually general wasting and sometimes extreme emaciation. On the other hand it is not uncommon to find a well developed layer of subcutaneous fat in a patient who has died of diabetes.

(2) *Brain*—In some cases where coma supervened before death congestion and œdema of the brain were common signs with marked thickening of the membranes and wasting of the convolutions in some cases. The choroid plexus may be congested and thickened, tumours in the region of the fourth ventricle and the medulla may be found.

(3) *Spinal cord*—Dilatation of the central canal enlargement of the perivascular sheaths and localized softening may be found due probably to secondary nutritive changes. Tumours of the cord have sometimes also been found.

(4) *Heart*—The heart muscles are often found to be pale soft or even distinctly fatty. Arteriosclerosis is fairly common. The blood sometimes shows signs of distinct lipæmia.

CHAPTER VII

DIAGNOSIS

The diagnosis of true diabetes mellitus is often an easy matter when the patient presents the usual signs and symptoms. But there are many cases in which considerable difficulty is experienced and elaborate laboratory methods of diagnosis are necessary. Some of these patients complain of unusual symptoms and the diagnosis of diabetes often comes from the ophthalmologist, dentist, neurologist or dermatologist whom the patient had occasion to consult for his ailments. The author had many patients referred to him like this who did not have the usual classical symptoms but on detailed study proved to be cases of true diabetes and the unusual symptoms which had led them to see an ophthalmologist, dentist or other specialist cleared up under treatment of diabetes alone.

The mere presence of sugar in the urine does not justify one making a diagnosis of diabetes* though in practice it is safer to treat him as a diabetic until the contrary is proved by clinical and laboratory tests. We know there are several conditions other than diabetes in which one may have transient or intermittent glycosuria. Exophthalmic goitre, diseases of the thyroid gland, excessive thyroid medication, acromegaly, cerebral tumour, gall stone, cirrhosis of the liver (specially of the infantile type), renal glycosuria, etc. are common examples.

In renal glycosuria the threshold level of the kidney for glucose is lowered so that the patient has glycosuria often with a normal blood sugar level. This condition can

* It should be remembered in this connection that the urine which is not necessarily glucosuric is not necessarily glucosuric.

be brought about experimentally in normal individuals by injection of Phloridzin

Renal threshold

The term renal threshold may be defined as that concentration of sugar in the blood which must be reached before glucose is eliminated in the urine. The normal threshold value for glucose is generally assumed to be about the level of blood sugar at 0.180 per cent.

It should be realized that this threshold level manifests itself in wide individual variations under certain conditions. The renal threshold is usually *elevated* in nephritis, arteriosclerosis and in long standing cases of diabetes. In one of the author's cases blood sugar value as high as 0.450 per cent was seen without co-existing glycosuria.

The renal threshold is lowered in cases of renal glycosuria. Some of the patients with renal glycosuria pass sugar in the urine for nearly the whole life, the glycosuria apparently doing them no harm. It has been found that most of these patients who come for investigation have a low renal threshold, i.e. they pass sugar in the urine with a normal or even subnormal blood sugar. In two respects only these people are likely to come to any harm, namely first that they are usually refused by the insurance companies which labour under the idea that glycosuria invariably means diabetes and secondly that when they happen to consult an inexperienced doctor for this innocent glycosuria they are often adjudged to be true cases of diabetes and are subjected to rigorous treatment. In the old methods of treatment by diet and drugs not much harm could come to these patients except perhaps some loss in weight due to unnecessary low dieting and some personal discomfort but since insulin has come into general use the aspect of these unfortunate cases has taken a turn for the worse and the author could testify to several cases of such patients who were brought to a pitiable condition owing to irresponsible or uncalled for treatment by insulin.

The diagnosis of true matter when the patient symptoms. But there are difficulty is experienced a of diagnosis are necessary of unusual symptoms and comes from the ophthalmologist whom the patient has ailments. The author him like this, who did not but on detailed study, and the unusual symptom ophthalmologist denies under treatment of diabetes.

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* It should be remembered reduces an alkaline copper solution only contain sugar. Vide instances in the urine their the *Indian Medical Gazette*.

Note. —

(1) How the rise of the blood sugar corresponds to the meals taken

In a normal healthy individual the maximum rise of blood sugar takes place between $\frac{1}{2}$ to 1 hour after the meal is taken. It comes down to normal level long before the next meal is due.

In a mild case of diabetes the maximum rise of blood sugar takes place $1\frac{1}{2}$ hours after the meal is taken. It comes down before the next meal is due, but is often much above the original level.

In severe cases of diabetes the blood sugar after the meal is taken, goes on rising and it does not usually get a chance of coming down before the next meal is due.

(2) The blood sugar is at its lowest level in the early morning before the individual has any food—the fasting level of blood sugar as it is called.

(3) The mild cases of diabetes are often sugar free in the morning and may also have a normal blood sugar level.

The shadowed areas in the chart represent the blood sugar above the kidney threshold (about 0.18 per cent), where sugar appears in the urine.

It has already been said that a normal healthy individual has a high capacity for the utilization of carbohydrates and large quantities of carbohydrates are ordinarily oxidized in the system without giving rise to glycosuria. Generally speaking, glucose excretion in the urine cannot take place until the concentration of sugar in the blood goes beyond 0.18 per cent or thereabout—this level of blood sugar concentration, as stated before, being termed 'renal threshold level' or the 'leak point for glucose'. We have already seen how difficult it is to raise the blood sugar in a normal healthy individual above the renal threshold because as soon as the blood sugar reaches near the threshold level the sugar storage mechanism intervenes and prevents further rise of the blood sugar.

In the case of the potential diabetic, or in cases of mild diabetes things are quite different. The power of carbohydrate utilization and storage in these individuals are deficient in varying degrees and thus the effect of the ingestion of glucose on the blood sugar level of these patients differs markedly from that in normal healthy individuals.

and this difference, as elicited by glucose tolerance tests has been utilized as a basis of investigation

The introduction of micro-chemical methods of blood analysis has rendered possible the repeated estimation of the blood sugar content at frequent intervals after the ingestion of glucose thus giving us an opportunity to study how the patient is responding to the sugar ingested. This test would not only differentiate a non-diabetic individual (who for some reason or other is passing sugar in the urine) from a true diabetic but would often help us in diagnosing the disease in the pre-diabetic stage

Glucose tolerance test

The procedure for a GLUCOSE TOLERANCE TEST is given below

Preparation of the patient—There should not be a too rigid restriction of the patient's diet prior to doing the glucose tolerance test. The test should preferably be done with the previous diet of the patient unrestricted. The morning (about the breakfast time i.e. 12 to 15 hours after the previous night's meal) is the best time to do it when the digestive activity is at its minimum. The patient should as far as practicable be at perfect physical and mental rest.

Before doing the test the patient empties his bladder and the urine is collected, measured and examined for sugar. At the same time a sample of blood is taken and its sugar content estimated. This is known as the 'fasting level' of blood sugar.

The patient is now given 50 to 100* grammes of glucose dissolved in 3 to 4 oz. of water. Half an hour after the glucose is given another sample of blood is taken and examined and this is repeated every half an hour for the

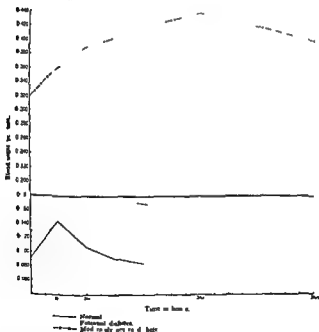
* According to the author blood sugar curves for diagnostic purpose can be obtained by the administration of 50 grammes of glucose and this amount is ordinarily used for routine work in the average adult cases.

next 2 or 3 hours. Specimens of urine are collected and examined preferably every hour.

In the average healthy normal individual the concentration of sugar in the blood usually rises after the ingestion of glucose from the initial fasting level of about 0.1 per cent to a maximum of 0.14 to 0.15 per cent within one half to one hour and thereafter it goes down to the normal level within an hour or thereabout (*vide* Chart IV). Variations of course occur but as a general rule it may be taken for granted that the maximum concentration of blood sugar

CHART IV

Blood sugar curves in glucose tolerance tests



in the normal individual is to be looked for within one hour after the dose of sugar has been taken. This highest point

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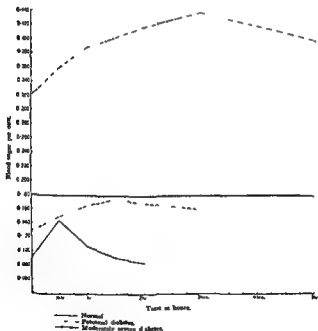
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Blood sugar curves in glucose tolerance tests



in the normal individual is to be looked for within one hour after the dose of sugar has been taken. This highest point

in the blood sugar concentration varies in different individuals but the safe maximum normal limit may be fixed at 0.17 per cent. As soon as the blood sugar level has reached this concentration the sugar storage mechanism comes into operation which abstracts sugar from the blood more quickly than it is absorbed and converts it into glycogen. The mechanism for this is very efficient in the normal healthy individual. The author tried four half hourly 50 gramme doses of glucose on himself but he was unable to force the blood sugar to go above 0.165 per cent.

As soon as the storage mechanism intervenes and the tissues and the liver begin to abstract sugar from the blood storing it as glycogen the blood sugar falls abruptly and within an hour and a half after the ingestion of sugar it comes down to normal or sometimes below the normal level.

Summarizing the results of the glucose tolerance test in a healthy normal individual we find that —

(1) The fasting blood sugar level is normal

(2) The maximum rise of blood sugar after 50 grammes of glucose have been ingested is within 1 hour and is not above 0.17 per cent

(3) The drop of the blood sugar to the normal level takes place within 1½ hours after the glucose is taken

(4) No glycosuria occurs

Now if the test is done in a case of *potential diabetes* we are likely to meet with the following results —

(1) The fasting level of blood sugar may be normal or slightly higher

(2) The blood sugar after a test meal of 50 grammes of glucose will however a the maximum
rise of blood sugar will tak in interval
than in the normal. The a very
near to at or , and
the level 7 hrs e
(3) 2 " not
abrupt

(4) The results drawn on a graph paper will show a long drawn out flat top blood sugar curve which is suggestive of a delayed carbohydrate assimilation (*vide* Chart IV)

The result of the glucose tolerance test in a case of *true diabetes* is very striking

(1) The blood sugar goes on rising and the maximum rise (sometimes reaching a very high figure) may not take place till the end of 3 or 3½ hours after the ingestion of glucose

(2) The fall of blood sugar also takes place slowly the original level of blood sugar (i.e. the level before the ingestion of glucose) not usually being reached till the end of 5 or even 6 hours according to the varying degrees of defect in the storage mechanism

(3) As a matter of fact the severity of diabetes can be gauged by the type of curve obtained after the glucose ingestion

(4) The kidneys actively excrete glucose all the time and the amount of increase of sugar in the urine after the dose of glucose is an additional evidence of the nature and severity of the case (*vide* Chart IV)

Thus we see that the glucose tolerance test if properly done and interpreted is not only one of the best and quickest methods of differentiation between a non diabetic and a diabetic individual but it also helps us in getting an idea of the nature and severity of the disease if the case proves to be one of diabetes

A few practical points for consideration

There are however a few practical points which must be taken into consideration in properly adjudging and interpreting the results of the test. For example the previous diet of the patient appears to the author to be a very important factor. It has for instance been definitely found that if a diabetic patient lived on a very low carbohydrate diet for several days before the test or starves himself for

two or three days prior to submission to the test the hyperglycemic response to the ingestion of glucose will be much more marked than if the patient had lived on a more liberal carbohydrate diet previous to the test and the results thus obtained will give us a false impression about the nature and severity of the case.

The evidence that starvation causes a lowering of carbohydrate tolerance even in normal individuals has further been found by the author in a recent work while engaged on metabolic studies in starvation cases during the last Bengal Famine 1913*. Among other interesting findings the author was able to show that short but acute starvation caused a marked lowering of the carbohydrate tolerance. Glucose tolerance tests done on these cases showed that in the majority the blood sugar curves obtained after a glucose meal simulated diabetic curves of varying degrees of severity. Prolonged malnutrition on the other hand was found to cause a defective absorption of glucose from the alimentary tract resulting in an almost straight blood sugar curve after the glucose meal. Blood sugar curves of a similar nature were also obtained in cases of sprue and acute anaemia.

* Working on this question namely the effect of the duration of fast on hyperglycemic response after glucose ingestion Staub came to the conclusion that the maximum glucose tolerance (or in other words the minimum hyperglycemic response to glucose) was obtained 14 hours after the previous meal and that the glucose tolerance began to decrease gradually as the period of fasting was increased. The best time to do the glucose tolerance test therefore, is about breakfast time about 14 to 15 hours after the previous night's meal. It is also evident to us that the patient should not be on a too rigid diet prior to being submitted to the glucose tolerance test. It is interesting to note here that the diabetic patient applying for an insurance policy

* A preliminary study of the Locomotor changes in starvation cases. Indian Journal of Medical Research 34: 1 May 1946

who thinks he can elude the doctor either by fasting or living on a very rigid diet before appearing for the test defeats his own ends

The effect of a low carbohydrate diet on the carbohydrate tolerance of the diabetic patient will be further discussed in the chapter dealing with the dietetic treatment of diabetes

Illustrative Cases

The following results were obtained by glucose tolerance tests on a few typical cases and are inserted below by way of illustration —

Case I—A P T aged 45

Refused by insurance companies several times for glycosuria which happened to be intermittent. No physical signs and symptoms of diabetes. No glycosuria occurred after a dose of 50 grammes of glucose

The result of the glucose tolerance test was as follows

	Per cent
Blood sugar before giving glucose	0.081
1 hour after 50 gm. of glucose	0.140
1	0.150
2 hours	0.081

Interpretation of result—The individual behaved exactly like a normal person. Sugar storage mechanism perfectly normal

Case II—E P

Intense sciatica for 10 or 15 days. Urine showed a trace of sugar. Another brother had slight glycosuria and albuminuria for a long time

The result of the glucose tolerance test was as follows

	Per cent
Blood sugar before giving glucose	0.105
1 hour after 50 gm. of glucose	0.116
1	0.140
2 hours	0.105
Urinary sugar before test	Nil
2 hours after 50 gm. of glucose	Traces

Interpretation of result—The blood sugar curve was perfectly normal but the kidney threshold was lower than normal

The case is one of *renal glycosuria*

Case III—P S, aged 29

Was excessively stout Referred to the author by an insurance company for over weight

The result of the glucose tolerance test was as follows

	Per cent
Blood sugar before giving glucose	0 108
½ hour after 50 gm of glucose	0 175
1	0 167
2 hours	0 1 5
Urinary sugar before test	Nil
2 hours after 50 gm of glucose	Nil

Interpretation of result—Definite defect in the sugar storage capacity The blood sugar continued to rise even at the end of 2 hours and nearly reached the threshold limit

This condition in a young man should be looked upon with suspicion as a *pre diabetic* stage

Case II—J C F, aged 32

Had kept very good health till about a month previous to examination when suffered from a crop of boils No clinical signs and symptoms of diabetes

The result of the glucose tolerance test was as follows

	Per cent
Blood sugar before giving glucose	0 110
½ hour after 50 gm of glucose	0 14"
1	0 176
2 hours	0 18"
Urinary sugar before test	Nil
2 hours after 50 gm of glucose	0 9

Interpretation of result—The sugar storage mechanism was definitely defective and this happening in a young man was indicative of *early diabetes*

Case V—P R R, aged 35

Refused by insurance company for glycosuria No visible symptoms present but on close questioning the

The result of the glucose tolerance test was as follows

	Per cent
Blood sugar before giving glucose	0.280
1 hour after 50 gm of glucose	0.340
1	0.30
2 hours	0.470

The urine before the test showed 2.4 per cent sugar which rose to 0 per cent 2 hours after 50 gm of glucose

Interpretation of result—Sugar tolerance markedly defective. The initial hyperglycæmia was fairly marked. The hyperglycæmia resulting from the ingestion of 50 gm of glucose was well marked and persisted for an abnormally long period provoking but a poor response from the sugar storage mechanism. There was a sharp increase of glycosuria 2 hours after the glucose meal.

Such a marked diminution in sugar tolerance indicated a fairly severe type of diabetes mellitus.

We thus see that the glucose tolerance test, if properly done and interpreted is one of the most valuable and indispensable means for determining the nature of the glycosuria one is called upon to deal with. It gives us a satisfactory clue as to whether the glycosuria is diabetic in origin or otherwise and is also indicative of the degree of severity if the glycosuria proves to be diabetic in origin.

Correct interpretation of results

A word of caution should be given regarding the correct interpretation of the results of the glucose tolerance tests. Mention has already been made about the influence of the previous diet of the patient on the results of the test. Among other factors which may also seriously affect the response of the diabetic individual to the glucose meal may be mentioned—severe infections of any kind toxic ingestion of thyroid extract previous administration of insulin etc. These factors should be kept in mind while interpreting results.

It should also be borne in mind that apart from diabetes certain other conditions may give rise to abnormal findings after a glucose tolerance test the principal amongst them being diseases of the liver hyperthyroidism hypertension nephritis acute starvation sprue acute anemia etc Table III given below includes averages obtained in a number of these conditions In interpreting the results of glucose tolerance tests therefore all these factors should be borne in mind and the diagnosis must be based upon evaluation of as much evidence as is available in each individual case

TABLE III

Average Blood sugar values following administration of 50 Gms of glucose

	Blood-sugar—Mgs per 100 c c						Ur ne sugar
	Fa t ng	1/2 hour	1 hour	1 1/2 hours	2 hours	3 hours	
Acute starvation	85	150	200	210	215	215	Traces
Prolonged Malnutrition	71	72	72	72	75	9	N l
Sprue	96	96	96	90	90	91	N l
Hypertension	110	170	180		160	130	N l
Nephritis	140	180	200		185	185	N l
Hypertension	100	200	150		170	110	N l or traces
Hepatic lesions	156	195	180	165	125	130	N l
Lag storage curve	100	200	140	100			+

It would not be out of place to mention in this connection that the estimation of the cholesterol content of the blood* (*vide* Chapter VIII) in cases of diabetes gives a valuable index as regards the severity of the case and its prognosis. The estimation of the inorganic phosphate content of the blood after a glucose meal as evidenced by the recent work of the author† also gives much valuable information as regards the rate of utilization of sugar in the tissues

* *J. Biol. Chem.* 124: 243, October 1936

† *J. Biol. Chem.* 124: 243, January 1939

The result of the glucose tolerance test was as follows

	Per cent
Blood sugar before giving glucose	0.780
½ hour after 50 gm of glucose	0.340
1	0.30
2 hours	0.40

The urine before the test showed 2.4 per cent sugar which rose to 6 per cent 2 hours after 50 gm of glucose

Interpretation of result—Sugar tolerance markedly defective. The initial hyperglycæmia was fairly marked. The hyperglycæmia resulting from the ingestion of 50 gm of glucose was well marked and persisted for an abnormally long period provoking but a poor response from the sugar storage mechanism. There was a sharp increase of glycosuria 2 hours after the glucose meal.

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It should also be borne in mind that apart from diabetes certain other conditions may give rise to abnormal findings after a glucose tolerance test the principal amongst them being diseases of the liver hyperthyroidism hypertension nephritis acute starvation sprue acute anemia etc Table III given below includes averages obtained in a number of these conditions In interpreting the results of glucose tolerance tests therefore all these factors should be borne in mind and the diagnosis must be based upon evaluation of as much evidence as is available in each individual case

TABLE III

Average Blood sugar values following administration of 50 Gms of glucose

	Blood sugar—Mgs per 100 c c						Urine sugar
	Fasting	½ hour	1 hour	1½ hours	2 hours	3 hours	
Acute starvation	85	150	200	210	215	215	Trace
Prolonged Malnutrition	71	72	72	72	75	79	Nil
Sprue	98	98	98	90	90	94	Nil
Hypertension	110	170	180		160	130	Nil
Nephritis	140	180	200		185	185	Nil
Hyperthyroidism	100	200	150		120	110	Nil or trace
Hepatic diseases	156	195	180	165	155	130	Nil
Lag storage curve	100	200	140	100			+

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* *Indian Journal of Medical Research* 24 2nd October 1938

† *Indian Journal of Medical Research* January 1939

CHAPTER VIII

BLOOD SUGAR AND BLOOD LIPIDS

Normal Fasting blood sugar level

As a result of a very large number of blood sugar determinations on people of different races during the last 25 years the author has come to the conclusion that the blood sugar level of healthy normal Indians after an over night fast is remarkably constant the average value being 100 mgs per 100 cc of blood with individual variations from 80 to 110 mgs. This would also show that the blood sugar level of healthy normal Europeans does not differ materially from that of Indians and that race *per se* has no influence on the blood sugar level *.

A value of 70 mgs on the low side and 120 mgs on the high side has sometimes been obtained these being considered as a low or high level normal value. A fasting blood sugar value of over 120 mgs per 100 cc should be viewed with suspicion.

The total amount of sugar present in the circulating blood is about 5 grammes.

Micro chemical methods of blood sugar estimation—The micro chemical method of blood analysis was introduced by Bang in 1913 resulting in a widespread clinical application of blood sugar determination. Even such a small amount of blood as 0.1 cc (which can be obtained from a finger prick) is now sufficient for an accurate estimation of blood sugar.

* *Banc J P Trans F E & T M* Seventh Congress
p. 150

*Sugar content in the capillary (arterial) and the venous blood **

It is now common knowledge that the sugar content of the capillary (arterial) blood represents such an amount of glucose as has been supplied to the muscles and tissues and thus would under certain conditions be higher than the sugar content of the venous blood which represents the remaining amount of glucose after a portion has been eliminated or utilized during its passage through the tissues

In healthy normal individuals the initial (i.e. fasting) level of sugar in both the capillary and the venous blood has been found to be practically identical but after the ingestion of glucose the rise in the sugar content in the capillary (arterial) blood is more rapid and pronounced than in the venous blood. This is chiefly due to direct absorption of the glucose from the intestines and partly according to some to hepatic glycogenolysis i.e. liberation of the glucose from the glycogen store house of the liver. The sugar content of the venous blood as has already been stated would naturally be somewhat lower because during its passage through the tissues particularly the muscles some portion of the sugar is removed for the formation of muscle glycogen and for eventual utilization. The difference between the sugar content of the arterial and the venous blood (arteriovenous difference as it is called) specially after glucose ingestion therefore roughly indicates the rate of glucose utilization in the muscles and tissues.

But while in a normal healthy individual the fasting level of sugar content of both the capillary and the venous blood is practically identical it is not so in some diabetic conditions. The mechanism both of storage and utilization of sugar in the tissues being markedly defective (as a result of the disease) the fasting level of sugar in the venous

* Arterio Venous Sugar difference in Fasting mellitus—Boase J
I dan Jo rnal Medical Re III J I 1935

blood may be and often is higher than in the capillary blood. This fact has frequently been taken advantage of as a simple means of determining the nature and the severity of the disease.

Distribution of sugar in the blood

Until 1908 it was believed that the whole amount of sugar present in the blood was contained in the plasma and that the corpuscles contained no sugar at all. Michaelis and Rona in 1909 were probably the first investigators to demonstrate by experiments on dogs that blood corpuscles also contained sugar though according to them there was no constant relationship between the corpuscular sugar and the plasma sugar. The author made a study of the distribution of sugar in the blood of diabetic and non diabetic subjects* and has among other things come to the following important conclusions —

(1) That in normal healthy individuals the concentration of sugar both in the plasma and the corpuscles are almost identical

(2) That in diabetic subjects things are quite different. Here the plasma sugar is always higher than the corpuscular sugar

(3) That the increase of the plasma sugar over the corpuscular sugar in cases of diabetes mellitus happens according to the severity of the disease. In other words the graver the disease the higher is the ratio of the plasma sugar to the corpuscular sugar. This according to the author is due to the inability of the corpuscles to take in and utilize sugar from the surrounding plasma

(4) In the author's opinion the estimation both of the plasma sugar and the corpuscular sugar in cases of diabetes mellitus will give a truer and better indication of the nature of the disease than estimation of the whole blood sugar alone and the determination of the plasma

* Bose J P *Indian Medical Gazette* Vol LXXII No III page 415

corpuscular ratio will give a much better indication of the severity of the disease

(5) Administration of insulin in cases of diabetes mellitus increases the permeability of the corpuscles to sugar intake helps in the utilization and storage of sugar within their own walls and thus brings the plasma corpuscular ratio down to normal

Glycolysis in normal and Diabetic blood

That sugar gradually disappears from the blood if allowed to stand *in vitro*, has been known for a long time but on looking up the literature on the subject it appears that there is no uniformity of opinion among the different workers who studied this subject from different points of view

The problem of glycolysis of blood in normal subjects in the tropics attracted the attention of the author a few years ago when he was studying the effect of temperature and the different anti coagulants on glycolysis in normal blood *

It was found that the blood lost its sugar content if left at room temperature and the higher the temperature the more rapid was the loss of sugar. As a matter of fact it was found that in some of the samples the loss of sugar after the sample was left at room temperature for 6 hours was nearly 70%. This important factor not having been taken into consideration in the past gave rise to different and conflicting results when the same sample of blood was examined at different intervals after its collection

Another significant and important finding was that if the blood was left in cold storage the loss of sugar became negligible. It was also observed that if soda fluoride was used as an anti-coagulant instead of pot citrate or oxalate which are commonly used the loss of sugar even in ordinary

* Bose J. I. and De L. N. *Indian Journal of Medical Research*
30 Jan 1942

temperature was negligible even after 12 hours. This was a very important finding as it solved the problem of examination of samples of blood for sugar sent from distant places.

Experiments on diabetic blood* however showed that under similar conditions the samples of diabetic blood behaved absolutely differently from normal blood as regards the rate of glycolysis. The loss of sugar was found to be extremely slow and in some samples collected from severe cases of diabetes there was practically no loss of sugar even when the samples were left at room temperature for a considerable period. The rate of glycolysis in the blood of mild cases of diabetes however did not differ materially from that observed in normal cases.

It has also been observed that the rate of glycolysis of diabetic blood depended on the severity of the diabetic condition. The greater the severity the lower was the loss of sugar. This important and significant finding has since been utilized by the author as a factor in assessing the severity of the diabetic condition.

Regulation of the blood sugar level—the influence of the endocrine glands

We know that in a healthy normal individual the fasting level of the sugar content of the blood remains practically at a constant figure. It usually increases after each meal and decreases after the effect of the meal has passed away. The mechanism by which the amount of sugar in the blood is regulated and kept at a constant level is however a very complicated process. We know that there are two groups of ductless glands with antagonistic actions which control this mechanism. One group consists of the suprarenals, the thyroid and the pituitary; the

* Bose, J. P. and De U. N. *Indian Journal of Medical Research* 33 May 1945

tendency of each of the glands being to mobilize sugar into the blood and cause hyperglycemia. The other group known also as the opposing group consists mainly of the pancreas (and possibly the parathyroids) the internal secretions of which *ie*, insulin tend (expressed in simple language) to check the hyperglycemia. The secretions of the former group are influenced by the sympathetic system and those of the opposing group by the parasympathetic system.

For some time past the author has been working on the problem of the interrelationship of and the antagonistic action as between the above named endocrine glands in regard to their influence on sugar metabolism and several papers have been published on the subject*. It is not the object of this book to discuss them in detail. It will be enough to say for instance that adrenalin acts antagonistically to insulin and that this action is not a direct neutralization of insulin by adrenalin but an indirect one. Adrenalin is believed to act through the liver by converting liver glycogen into sugar and mobilizing it into the blood thus tending to raise the blood sugar level. Insulin on the other hand causes the excess of sugar in the blood to be taken up by the muscles which store it up as muscle glycogen for final utilization thus tending to bring the blood sugar level down. It thus becomes clear why adrenalin is a very useful antidote in the treatment of insulin hypoglycemia.

That there is some relationship between the action of the suprarenal bodies and the thyroid gland is undoubted though the evidence is not conclusive on the point whether this relationship is a direct one. Thyroid like the suprarenals acts antagonistically to insulin.

The adrenals as has just been said act through the splanchnic nerve and the hepatic plexus causing a release

* Dose J P *Transactions of the Society of Experimental Medicine* Vol III
p 335

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* Bose, J. P. and De U. N. *Indian Journal of Medical Research*
33 May 1945

action of the hormone of the anterior lobe of the pituitary gland seems to be one of insulin antagonism *i.e.*, it acts by opposing the effect of insulin in the tissue thus inhibiting its power of glycogen formation in the muscles (glycogenesis) and final utilization. It has also been suggested that the pituitary hormone secures its objective through the inter-mediation of the suprarenals.

To summarize the normal process of the regulation of blood sugar it thus appears that the concentration of sugar in the blood is the resultant of two main forces —

(1) Those which affect the liberation of glucose from the glycogen store house of the liver

We have seen that the main function of the hepatic glycogen is only to supply glucose to the circulating blood according to the changing needs of the organism and in this it is helped by the suprarenals and the thyroid in the maintenance of the blood sugar level. The hepatic glycogen unlike the muscle glycogen does not directly supply glucose for tissue utilization.

(2) Those which affect its withdrawal from the blood stream for deposit as glycogen in the tissues and its final utilization.

We know that during the metabolic activities in the muscles they draw upon their glycogen reserve to supply them with glucose for combustion, to make good the loss more glucose is abstracted from the circulating blood to be transformed into muscle glycogen and kept in store for future combustion in the tissues whenever required. This phase of carbohydrate metabolism is dependent upon the action of insulin* and it is this action of insulin that pituitrin appears to antagonise, *i.e.*, it depresses the glycogen formation in the muscles.

* In cases of diabetes mellitus where there is deficiency of insulin in varying degrees the excess of glucose in the circulating blood is incapable of being transformed into muscle glycogen or utilized in the tissues.

of sugar from the glycogen storehouse of the liver, thus tending to cause hyperglycemia. It is believed that the thyroid helps to intensify this action to a great extent. The author has shown by experiments on rabbits that when the thyroid is removed the animals react in a markedly less degree to adrenalin stimulation than before the operation.* Another very important observation made by the author was that these thyroidectomized rabbits became highly sensitive to insulin.

The results of the author's experiments tend to show that the absence or deficiency of thyroid secretion depresses the function of the adrenals to an appreciable extent but enhances the activity of insulin to a remarkable degree. Thyroidectomy probably depresses the functions of the chromaphil tissues. Normally thyroid secretion is believed to be a direct stimulant to the chromaphil tissues causing them to yield adrenalin to blood in large quantities and the excess of adrenalin thus secreted through such stimulation acts through the splanchnic nerve and the hepatic plexus and causes a release of sugar from the liver glycogen.

It thus appears that thyroidectomy alters the glycolytic response of the liver to adrenalin stimulation and hence enhances the activity of the insulin producing cells of the pancreas. Some observers have noted that the inhibitory action on the pancreas is removed to a large extent after thyroidectomy and that there is a distinct increase in the islet cells of the pancreas after the thyroid is removed. The thyroid like the suprarenals thus takes a considerable share in the regulation of the level of blood sugar.

The pituitary gland is also believed to take an important part in this connection. Cushing has shown that intravenous injection of extracts from both the anterior and the posterior lobes diminish the tolerance of experimental animals to glucose. It has already been stated that the

* Bosc J. P. *Indian Journal of Medical Research* 18 N. 1

While the value of limitation of fat in the diabetic diet was slowly gaining ground Newburgh and Marsh in 1920 showed exceptional courage in coming forward with their theory advocating high fat diet in the treatment of diabetes. They showed that diabetic diet containing as much as 200 grammes of fat daily was not only not injurious to the diabetic patients but that they improved considerably on such a diet. This was corroborated by Blatherwick who further showed that the fat content of the blood actually fell as a result of such treatment.

In view of such conflicting observations it was not surprising that the method of treatment of diabetes by high fat diet as advocated by Newburgh and Marsh was looked upon with fear (of acidosis) but the result of the treatment in causing marked clinical improvement negatived such apprehension. As a matter of fact efforts were made to discover the cause of this apparent anomaly and it was found that the real cause of the clinical improvement was not the high fat diet but the principle of under nutrition which was combined with it. The total calories allowed by this fat diet was only 1 000 in the beginning and the usual maximum reached was about 1 800.

Bliss in 1926 further showed that if the metabolic activities in the diabetic were kept low the clinical symptoms ameliorated and the lipemia vanished even when the patients took as much as 200 grammes to 250 grammes of fat daily.

It must be admitted that though the principles of dietetic treatment as advocated by these authors are not applicable to-day their work deserves recognition in the sense that they have shown that when diabetic patients are put on large quantities of fat they do not develop acidosis and even when they are protected by under nutrition by a high caloric diet with the minimum protein allowance the application of this form of treatment in the future of the diabetic

BLOOD LIPIDS IN DIABETES *

For several years past increasing interest has been taken on the significance of cholesteremia in diabetes and the part it plays in the prognosis and complications of the disease. In the old days when phlebotomy used to be one of the methods in the treatment of diabetes milkiness of the diabetic blood used to be a common finding in the severe cases especially those with associated nephritis. Later on the cream which separated out from the milky serum was recognised to be fat and the condition was recognized as lipæmia.

See in 1909 was probably the first to draw pointed attention to the fact that similar lipæmia could be produced in experimental diabetes in animals by the removal of the pancreas. This has since been corroborated by other workers.

Professor Bloor who had done a considerable amount of work in connection with the fat content of blood in health and disease definitely showed that the lipoid (fat) content of the blood in the average diabetic was much higher than in the normal. This was corroborated by Gray and others.

Bloor's findings thus led to important and interesting consequences. Joslin in 1917 went more deeply into the problem and concluded that the diabetic state was responsible for producing some defect in the mechanism for the transportation disposal or metabolism of fat. It was also shown experimentally that feeding diabetic patients with fat increased the lipoid content of the blood. Emphasis was thus laid on the fact that limitation of fat in a diabetic diet would be advantageous. The necessity of its total dietary regulation in the treatment of diabetes is advocated by Allen in 1919 appears to be a direct result of such a finding.

* Bosc and De L. *dan Journal of Medical Research* 24 2nd October 1936

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It must be admitted that though the principles of dietetic treatment as advocated by these authors are not applicable to-day their work deserves recognition in the sense that they have shown that when diabetic patients are put on large quantities of fat they do not develop acidosis and coma if and when they are protected by under nutrition by having a low caloric diet with the minimum protein allowance but how far the continuation of this form of treatment for a long period will affect the future of the diabetic is a controversial and disputed point.

Cholesterol content of plasma in normal subjects

In healthy normal individuals the average cholesterol content of the plasma has been found to be 140 mg per 100 c.c. the range of variation being 120 mg to 160 mg per cent. It has also been observed that the cholesterol content of the blood (plasma) of healthy normal Indian subjects does not differ materially from the standard European and American figures thus showing that like blood sugar, the plasma cholesterol does not show any material racial difference.

Cholesterol metabolism

There is a good deal of controversy, with regard to the identity of the organ concerned in the metabolism of cholesterol. It appears to us that the consensus of opinion tends to support the theory that it is the reticulo-endothelial system which governs and regulates this metabolism i.e. it tends to remove cholesterol from the blood when it is in excess and return it to the blood when cholesterol content becomes low in the blood. Thus according to this view, a persistent hypercholesterolemia indicates a condition of hypoactivity of the reticulo-endothelial system and a persistent hypocholesterolemia indicates a condition of hyperactivity of the system.

According to all observations the liver appears to play an important part in the intermediary metabolism in the elimination of cholesterol the chief source of elimination appearing to be the bile through the agency of polygonal cells of the liver.

Cholesterol metabolism in diabetes

It has been stated that a condition of hyperlipemia can be produced in experimental diabetes in animals after removal of the pancreas. It has also been stated by workers that lipæmia is rather constantly associated with diabetes mellitus, though as has been sugg

Slyke and Peters in 1931 these may only mean an abnormal localization of lipoids in the blood rather than an impairment of the metabolic process

It has also been suggested that diabetic lipemia is indicative of a demand for metabolism of fat because of the unavailability of carbohydrate fuel. This hypothesis appears to be reasonable in view of the fact brought out by several workers that the degree of hypercholesteremia is more or less an accurate indication of the severity of the disease. It appears to be particularly true in several untreated cases in some of whom extremely high figures (a few being above 1000 mg per 100 cc and several above 500 mg per cent) have been reported. Joslin has described a case of diabetic coma where the cholesterol content of blood was 1420 mg per cent. This case did not recover.

According to the observations made by the author the cholesterol content of the blood in diabetic subjects varies according to the severity of the diabetic condition. Another observation made was that the extent of hypercholesteremia bears little relationship to the state of hyperglycemia. Cases showing extreme cholesterol values may show only moderate hyperglycemia. Extreme hyperglycemia on the other hand may be associated with normal cholesterol content of the blood.

It was further observed that the majority of the cases of diabetes showing a normal cholesterol value of the blood did not have any complications though the hyperglycemia in some of them was well marked whereas cases showing moderate or marked hypercholesteremia almost invariably had complications and the response to treatment was usually unsatisfactory.

Arteriosclerosis was found to be a fairly common complication in chronic diabetes the exciting cause in most cases being hypercholesteremia.

We are thus faced with the interesting and important question as to whether there is any direct relationship

characteristic needle shaped cholesterol crystals and fatty acids which sooner or later combine with calcium. These calcium soaps become calcareous giving rise to an atheromatous condition of the artery.

We thus see how arteriosclerotic changes in the chronic diabetic occur helped by a state of hypercholesteremia predisposed no doubt by a state of persistent hyperglycemia. We cannot do better than quote Joslin who in his inimitable way states that with an excess of fat (obesity) diabetes begins and from an excess of fat the diabetics die—formerly of acidosis now of arteriosclerosis. Arteriosclerosis now causes more than one half of all diabetic deaths.

CHAPTER IX

PRINCIPLES OF DIETETICS AND THEIR APPLICATION IN THE TREATMENT OF DIABETES

We know that food is required for two main purposes

(1) To supply materials for the growth of the body and to replace the loss that is constantly taking place due to muscular and other activities

(2) To supply energy for conversion into heat and work

The six nutritive principles of food are —

- (1) Protein
- (2) Carbohydrates
- (3) Fats
- (4) Minerals
- (5) Water
- (6) Vitamins

These are contained in varying proportions in the different foodstuffs some of which are composed of not more than one or two of these principles

Proteins or nitrogenous food (such as fish meat eggs milk cheese *chhana dal* etc) — The building up of the muscles and other tissues of the body and the repairing of their loss are the main functions of the protein foods. The lack of the requisite amount of protein in one's diet leads to wasting a low state of health and diminished resisting power of the body tissues. Neither fats nor carbohydrates can take any part in this process of tissue building and repairs

Carbohydrates — These mainly consist of sugars and starches being chemically composed of carbon hydrogen and oxygen the proportion of hydrogen and oxygen being the same as in water. Their chief function is to produce

heat and energy for work. Carbohydrate foods also take part in the formation of body fat and this is one of the reasons why excessive indulgence in rice potatoes and sweet meat makes one stout.

Fats—This group consists of butter ghee and other animal fats and vegetable oils. These like carbohydrates do not contain any nitrogen but are composed of carbon hydrogen and oxygen only though the proportion of oxygen in fat is much less than in carbohydrates. The main function of fats in one's food is to produce heat and energy like the carbohydrates they are no good in tissue repairs. The fats however do not burn in the system as readily as the carbohydrates but they produce more than double the quantity of heat.

In addition to the above different kinds of minerals water and vitamins play an important part in the nutrition of the body and in activating and controlling its metabolism.

A normal diet should consist of a mixture of all these principles of food in due proportions which vary according to rice climate age sex body weight and occupation in life.

Of the first three classes of food mentioned above the proteins being the only nitrogenous food are mainly responsible for the repair of body waste and for the building up of muscles and other tissues. Without going into details as to the method by which the amount of protein required in a normal state of health is determined it may be stated that the average requirement for an adult person should be about $1\frac{1}{2}$ grammes per kilo of his body weight. Roughly speaking, an average healthy adult doing ordinary work requires about 90 grammes of protein per day.

The amounts of carbohydrates and fats vary widely according to rice climate work to be done etc. but between them they must supply the total amount of energy required by the individual. Proteins too produce energy but to a much less extent and are not generally drawn upon

if the supply of the other two kinds of energy producing food is sufficient

Caloric value of food

The potential energy contained in the first three proximate principles of food is measured by the amount of heat they produce on complete combustion in a calorimeter. It has been estimated that 1 gramme of fat produces 9.3 calories of heat while 1 gramme of protein and 1 gramme of carbohydrate produce 4.1 calories each. A calorie is the unit of heat and is the amount of heat required to raise the temperature of one kilogramme of water by 1°C , i.e., 4 lbs of water about 1°F .

Caloric requirement

The exact amount of calories required by an individual per day varies according to his body weight and the amount of work he has to perform, that is the amount of calories he expends. It has been estimated and as a working rule it may be taken for granted that an individual at rest requires about 30 calories per kilo (2.2 lbs) of his body weight per day and if the requisite quantity is not supplied by food it is produced by the process of the internal combustion of the tissues of the individual leading to wasting of the body.

We thus see that for supplying heat and energy the requisite amount of calories must be supplied by food and that the utmost use should be made of fats on account of their ability to supply more calories per gramme than either proteins or carbohydrates. But the use of fats is limited by the consideration that without the aid of carbohydrates they cannot be completely oxidized. It has been rightly stated that the fat of food burns in the flame of carbohydrates within the system and in cases of diabetes it is a well known fact that a defective fat metabolism accompanies subnormal carbohydrate combustion. The right proportion of fat to carbohydrate in a normal diet has been

estimated as 1 to 6. The standard amounts of the various constituents of an average diet as given by HUTCHINSON are given below —

Proteins	100 grammes
Carbohydrates	450
Fat	75

Working out the caloric value of the above diet we get the following figures representing the number of calories daily required by an adult healthy man engaged in ordinary work —

Protein	100 gm × 4.1 =	410 calories
Carbohydrates	450 gm × 4.1 =	1845 calories
Fat	75 gm × 9.3 =	697 calories
Total		2952 calories

Besides the standard amounts of the various constituents stated above a well balanced normal diet should contain requisite amount of minerals and an adequate supply of vitamins.

The average daily mineral requirement of a normal healthy individual is considered to be the following —

Calcium	10 mg
Iron	0.2 mg
Phosphorus	15 mg
Magnesium	0.3 g
per kg. of body weight	

Dietetic treatment of diabetes

Coming now to the dietetic treatment of diabetes we see that the fundamental principle underlying it is the administration of such an amount of carbohydrate food as is within the tolerance or limits of utilization of the patient so as to give rest to the pancreas.

Much laborious investigation for finding out a purely dietetic treatment of diabetes has been carried out all over the world and many empirical systems of treatment (such as skimmed milk, potato, oatmeal cures etc.) have come in

gone. A rational method of dietetic treatment applicable to all classes of diabetes has yet to come though lately much research work has been done in this direction. The main idea of the dietetic treatment of diabetes now lies in the fact that the metabolism must be kept low and therefore the patient should be given only such an amount of food as is necessary to meet the minimum metabolic requirement of his body so as to prevent drawing upon his own tissues. WILDER and his associates after a prolonged study came to the conclusion that the power of the glucose utilization of the patient varied inversely to his metabolic rate i.e. when the metabolic rate was at a minimum the glucose utilization was at the maximum and vice versa.

It should never be forgotten that though curtailment of diet is necessary to lower the metabolic activities, the patient should be given enough food to supply him with his minimum requirements and to keep him in proper health otherwise the patient will draw upon his own body protein and fat and this state of affairs if continued for a long time may result in disaster.

According to the old principle of treatment of diabetes by diet a high protein diet was usually given. We know now that this method of treatment is not without its danger as acidosis and coma (which are dangerous complications) will often be a direct result of this method of treatment. Protein yields not only a large percentage of glucose (58 per cent) but also a high percentage of acids capable of causing acidosis. The increased metabolism and the increased nitrogen output in the urine observed under the old methods of treatment was due to the large nitrogen content of the diabetic diet.

Several eminent physicians having made extensive studies have founded different methods of dietetic treatment which are named after them. It is not necessary to go into them in detail but a brief outline of some of them would not be out of place.

Allen's treatment—Founded by Frederic M Allen of America who may be said to have revolutionized the treatment of diabetes in his time by introducing his system of starvation treatment

This method of treatment was very widely used at one time but owing to the tediousness of the course the majority of the patients could not be induced to continue it for any length of time and so the ultimate results were often unsatisfactory. This method of treatment is not much in use now.

Allen's treatment was based on experimental observations on dogs which were made diabetic by the removal of part of the pancreas. Allen found that the fate of these dogs as to recovery or death depended on the subsequent feeding they were subjected to. If ordinary diet was given the animals died within a short time but if a carefully restricted diet was given life could be indefinitely prolonged.

Graham's treatment—George Graham of St Bartholomew's Hospital in London working separately also came to the same conclusion as Allen. Essentially the principles of treatment in the two systems are the same differing only in minor details. This treatment is generally known as Graham's Ladder Diet.

Joslin's treatment—Dr Joslin of America in dealing with recent cases of diabetes adopts the following line of treatment—

(1) The patient is put on a diet containing about 20 calories per kilo of body weight with carbohydrate at 100 to 150 grammes protein 50 to 60 grammes and fat between 60 and 80 grammes.

(2) He is given 5 units of insulin before each meal if his urine shows at that time a red or yellow reduction with Benedict's test.

As soon as the glycosuria diminishes the total calories are increased by gradual addition of carbohydrate protein and fat in proper proportions. The increase of carbohydrate above 120 grammes should be done cautiously. As soon as the

The line ration' scheme of Lawrence—Lawrence introduced this system of measurement of diabetic diet in 1925 which has simplified the process of calculation both from the point of view of the doctor and the patient. By means of this simple yet varied diet scheme the busy practitioner is enabled to treat cases of diabetes without elaborate calculation of diet and food values and the diabetic patient is also able to vary his food to suit his taste. This form of dietetic treatment however has not found much favour among doctors and patients in this country the chief reason being that the nature of the food taken varies so widely in the different parts of the country (according to race religion etc.) that no form of fixed diet scale appears to be suitable.

The practical method of the scheme is as follows —

Each black line in the chart represents 10 grammes of carbohydrates and each red line represents $7\frac{1}{2}$ protein and 15 grammes of fat. One line ration is a complete line and consists of one black and one red portion and has a caloric value of 210 so that to get the total number of line of rations allowed to the patient one has to divide the total caloric requirement of the patient by 210. Any black portion can be added to any red portion to make one ration but two black portions or two red portions must not be combined to make a ration.

High carbohydrate diet

During the last few years there has been an increasing tendency to treat cases of diabetes with a much higher allowance of carbohydrates than has hitherto been done. As a matter of fact the type of diet as advocated by Samson Geylin and others differs very little from the normal diet. The principle underlying this system of treatment appears to be based on the idea that increased carbohydrate intake under certain conditions stimulate the islet cells of

the pancreas to increased activity whereas a very low carbohydrate diet lowers the tolerance of carbohydrates.

The consensus of the present day opinion is that if a diabetic patient is given less carbohydrate than his real tolerance allows the carbohydrate tolerance will gradually fall through disuse. It is also a recognized fact that once the carbohydrate content of the diabetic patient's diet is lowered to an extreme degree it is very difficult to raise it again.

The author's clinical experience has been that it is easier to get good results with an untreated diabetic than one who has been rigidly dieted before. Sweeney has definitely stated that there is a decrease in the patient's tolerance after a fat diet or starvation but an increased tolerance after a high carbohydrate diet.

The tendency of the present day treatment of diabetes mellitus thus appears to be to give a high carbohydrate but at the same time a low fat and a low caloric diet. The work of Rabinowitch of Montreal deserves special mention in this connection. Rabinowitch has definitely shown by experiments carried on for over four years that patients previously on a low carbohydrate high fat and a high caloric diet sometimes require less insulin when their diet is changed to the high carbohydrate low fat and low caloric diet.

Eason and Lyon (*Lancet* 1933) have confirmed Rabinowitch's findings and are of opinion that if the total calories are reduced by fat restrictions the dose of insulin may be reduced although the carbohydrate in the diet is doubled.

Author's Formula for the Calculation of Diabetic Diet

In order to ascertain the amount of various foodstuffs required by a diabetic individual various formulae have from time to time appeared. The author has devised a

simple but proportionate formula to calculate a diabetic diet under basal conditions resting on the assumption that a diabetic requires 30 calories per kilo of body weight at rest or with very light work. The weight of the patient in kilogrammes multiplied by 30 gives us the number of calories he requires (1 kilo = 2.2 lbs). This total caloric requirement divided by 15 gives the amount of fat the individual requires in grammes, the same divided by 15 gives the amount of carbohydrate in grammes and when divided by 30 gives the amount of protein in grammes.

Or

$\frac{\text{Calories required}}{15}$ fat in grammes

$\frac{\text{Calories required}}{15}$ - carbohydrate in grammes

$\frac{\text{Calories required}}{30}$ - protein in grammes

Let us take a concrete example

A diabetic individual weighing 70 kilos (15 stone) will require the following diet —

If a caloric requirement at rest or light work would approximately be $70 \times 30 = 2100$

$\frac{2100}{15}$ 140 would be the approximate amount of FAT required in grammes

$\frac{2100}{15}$ 140 would be the approximate amount of CARBOHYDRATE in grammes

$\frac{2100}{30}$ 70 would be the approximate amount of PROTEIN in grammes

The number of grammes of fat, carbohydrate and protein being thus ascertained the patient's diet is framed by the use of food tables (see Appendix II).

For the convenience of general practitioners three sets of diet suitable for a diabetic patient weighing about 70 kilos and having the approximate food values as detailed above are appended below —

Diet No 1—Suitable for a European or an Anglo Indian

Diet No II—Suitable for an Indian on mixed diet

Diet No III—Suitable for an Indian on purely vegetarian diet

Diet No I

Foodstuffs	Quantity
Breakfast—	
Tea with milk $\frac{1}{2}$ oz (without sugar)	1 or 2 cups
Bread	1 oz
Butter	$\frac{1}{4}$ oz
Egg	1 only
Bacon	1 oz
Tomatoes	2 oz
Lunch—	
Beef tea or Bovril	8 oz
Green vegetables	8 oz
Lean meat (Mutton)	2 oz
Ham	2 oz
Bread	2 oz
Grapefruit	2 oz
Coffee (without sugar) with milk oz	1 or 2 cups
Afternoon tea—	
Bread	1 oz
Butter	$\frac{1}{4}$ oz
Egg	1 only
Tea with milk $\frac{1}{2}$ oz (without sugar)	1 or 2 cups
Dinner—	
Clear soup	8 oz
Lean meat (mutton)	4 oz
Green vegetables	8 oz
Bread	2 oz
Apple	4 oz
Coffee (without sugar) with milk $\frac{1}{2}$ oz	1 or 2 cups
Custard {	Egg
	Milk
	Saccharine
Ghee or Butter for cooking	2 oz

Diet No II

Foodstuffs	Quantity
Early tea—	
Tea (without sugar) with milk	1 oz
Bread	1 oz
Butter	$\frac{1}{4}$ oz
Eggs	2
Breakfast—	
Atta Chapattis	2 oz
Green vegetables	8 oz
Fish (or meat)	3 oz
Dahi (unsweetened)	4 oz
Afternoon tea—	
Tea (without sugar) with milk	1 or 2 cups
Bread	1 oz
Butter	$\frac{1}{4}$ oz
Boiled vegetables	4 oz
Coconut kernel	2 oz
Dinner—	
Atta Chapattis	2 oz
Green vegetables	8 oz
Fish (or meat)	3 oz
Milk (1 cup)	6 oz
Ghee or butter (for cooking)	$2\frac{1}{2}$ oz

Diet No III

Foodstuffs	Quantity
Morning—	
Milk	8 oz
Almonds or Pistachios	2 oz
Noon—	
Atta Chapattis	2 oz
Dal	$\frac{1}{2}$ oz
Green vegetables	8 oz
Dahi (unsweetened)	4 oz

Foodstuff	Quantity
Afternoon—	
Chhanna	2 oz
Cocoanut kernel	2 oz
Boiled vegetables	4 oz
Dahi (unsweetened) made into Ghol	4 oz
Night—	
Loochies or Paratas	2 oz
Dal	1½ oz
Green vegetables	8 oz
Chhanna	2 oz
Ghee or butter (for cooking)	1 oz
Tea may be taken without sugar if desired	

The patient is put on one of these diets for a week. The total quantity of sugar excreted in 24 hours is estimated daily and this is subtracted from the available glucose in the diet*. This figure will roughly indicate the patient's tolerance for sugar.

On a diet calculated as above the average diabetic patient of the mild type usually becomes sugar free in four days and the blood sugar comes down to normal in about a week's time. If however the patient does not become aglycosuric or maintain the blood sugar at the normal level on such diet insulin treatment is usually indicated.

It should be remembered also that the diet outlined above allowing as it does only 30 calories per kilo of the patient's body weight should be considered to be only a basal diet i.e. it is enough for an average patient at rest.

* This includes as already stated 58 per cent of glucose derived from the protein and 10 per cent from the fat in addition to 100 per cent from the carbohydrate in the diet.

The total available glucose in the diet mentioned above would thus be as follows—

10% of 140 gm of fat	—	14 gm of available glucose
100% of 140 gm of carbohydrate	—	140
55% of 70 gm of protein	—	40
Total		194

The total glucose value of the diet is therefore roughly 194 grammes

but is insufficient for a person having to carry on his daily work and it is necessary that after the patient becomes sugar free and the blood-sugar comes down to normal, the carbohydrate content of the diet should gradually be increased (*keeping the protein and the fat content constant as far as possible*) so that the caloric value of the diet is gradually raised to about 35 calories per kilo of the body-weight and this, for all practical purposes should be enough to maintain an average person doing ordinary work (*maintenance diet*). The addition of carbohydrates in the diet should however be done gradually 10 grammes each time allowing a period of 4 or 6 days in between to watch the effect.

For a rough and ready guidance to patients and to enable them to make suitable additions of carbohydrates to their diets as stated above a diet list is appended. As each of the foodstuffs given in the table below contains approximately 10 grammes of carbohydrate in the quantities noted against each item the patients get a fairly good choice for selection according to their taste and requirement.

TABLE IV *

Foods containing approximately 10 grammes of carbohydrate in quantities noted against each

Food	oz	Food	oz
Cereal Products—		Sago	$\frac{1}{2}$
Rice (white)	$\frac{1}{2}$	Sooji	$\frac{1}{2}$
unshelled	$\frac{1}{2}$	Wheat flour (atta or Mandi)	
Barley	$\frac{1}{2}$	Milk and Milk Products—	
Bran	$\frac{1}{2}$	Dahi (unsweetened)	11
Maize	$\frac{1}{2}$	Milk	"
Crushed	$\frac{1}{2}$	Powdered milk	1

* 1 ounce for total portion of an ounce given in the following table may sometimes present difficulties but the following rough scale of weights with four annas into may often be found handy and useful. The

3	for annas 115	will approximately weigh	1 2 oz
4	"		2 5 "
5	"		3 2 "
"	"		3 3 "
8	"		3 4 oz

Foods containing approximately 10 grammes of carbohydrate in quantities noted against each—(contd.)

Food	oz	Food	oz
<i>Vegetables—</i>		<i>Fruits—</i>	
Carrot	4	Apples	2½
Green vegetables (average)	7	Guaia	3
Green mango	4	Papaya	3
Green peas	2	Pineapple	3
Marichaku	2	Panolo	3½
Onion	3	Orange	4
Plantain (green)	2½	<i>Nuts—</i>	
Potato	2	Chestnuts	1
Red pumpkin (kumra)	5	<i>Miscellaneous—</i>	
Raddish	5	Force	¾
Tomatoes	8	Grape nuts	½
Turnip	5	Horicks	1½
		Oatmeal	¾
		Shredded wheat	¾

Monotony of diets

Diabetic patients often complain of the sameness or monotony of their daily diet. A wise and intelligent person may with a little care and judgment greatly minimize this disadvantage. All that is necessary is to substitute one food occasionally for another with more or less similar food values. This can be done easily by consulting the food tables given in the appendix and taking different quantities of other food stuffs containing the same amount of carbohydrate or protein.

To enable patients to select such *equivalent* foods a list is appended below keeping 1 oz of bread, containing about 16 gramma of carbohydrate per ounce as a standard for comparison with other carbohydrate foods. The list indicates the approximate quantity in ounces of some of the other carbohydrate foods which can be exchanged for each ounce of bread. If only half an ounce of bread is required to be exchanged the quantity given in the list has to be halved.

TABLE V

Approximately 'Equivalent' Foods

Food	oz	Food	oz
<i>Starchy foods—</i>		<i>Mankachu</i>	3
Bread	about 1	Onions	5
Barley	, $\frac{3}{4}$	Peas (green)	, 3
*Chira (beaten rice)	$\frac{3}{4}$	Potatoes	, 3
Cream cracker biscuits	1	<i>Fruits—</i>	
Corn flour	$\frac{3}{5}$	Apple	4
Lence	$\frac{2}{5}$	Banana	2½
*Kho (fried paddy)	$\frac{3}{4}$	Guaia	5
Macaroni	$\frac{3}{4}$	Mango (ripe)	3
Mure (makol)	$\frac{3}{4}$	Orange	6
Muri (Tuffed rice)	$\frac{3}{6}$	Papaya	4½
Oatmeal	$\frac{1}{6}$	Pineapple	5
*Pice	$\frac{2}{3}$	Pumelo	5½
Sago	$\frac{2}{5}$	<i>Nuts—</i>	
Shredded wheat	$\frac{1}{2}$	Chestnuts	1½
Sooji	1	<i>Milk and Milk Products—</i>	
Wheat flour (malda or atta)	$\frac{3}{4}$	Milk	11
<i>Vegetables—</i>		Horlicks	¼
Beet	, 4	Ovaltine	1
Jack fruit seed	1½	<i>Miscellaneous—</i>	
Mango (green)	6	Sandwich (chicken)	1½

* Foods marked with asterisks should not be taken in excess.

CHAPTER V

INSULIN TREATMENT

THERE is no doubt that the discovery of insulin has completely changed both the outlook and the treatment of diabetes mellitus specially of the severer type. It has certainly helped to save many lives but at the same time a note of warning should be sounded regarding its exact place in the treatment of diabetes mellitus about which is much misconception still exists. Joslin very aptly says

Insulin is a remedy primarily for the wise and not for the foolish be they patients or doctors. One should never forget that insulin has its uses and abuses its potencies as well as its limitations and the misconception that unfortunately prevails viz that by resort to this treatment one is at liberty to have practically unlimited diet should be combated and condemned. The patient undergoing insulin treatment should be clearly made to understand that insulin is only a valuable adjunct to the dietetic treatment and that it can in no sense be considered to be a substitute for the other and that to get the full benefit of insulin treatment there must be a more or less constant relationship between the dosage of insulin and the quantity of the diet allowed in individual cases. Under no circumstances should insulin be given in large doses merely to satisfy the capriciousness of the patient. The unfortunate practice which prevails in some quarters of employing insulin in order to allow the patient satisfaction in controlled luxuries in the treatment and still by discarding the method of treatment increases the weight of the patient does not take into consideration the fact that all which is thereby

necessary increase in the metabolic activities of the patient brought on by this method of treatment is apt to cause further damage to the already damaged pancreas with the prospect of its being eventually destroyed thus necessitating the use of continually increasing dosage of insulin. Lawrence has very rightly said that this method is like adding another cylinder and extra horse power to a damaged motor thereby running the machine too fast for the damaged part and ultimately wearing it out altogether so that more and more horse power has to be added if the machine is to be kept going at all.

Another misconception, unfortunately prevalent even today is that once insulin is taken it has to be continued for a life time. The pity of it is that such misconception is responsible for driving many cases into the arms of quacks and dealers in secret medicines resulting in unnecessary suffering and hardship often ending in disaster. It should be made clear once for all that insulin never generates or develops a habit like the narcotic drugs and the literature is very full of evidence that when insulin is used judiciously the carbohydrate tolerance of the patient improves so considerably that the dose of insulin may gradually be reduced until it may ultimately be stopped.

Insulin Treatment

The principle underlying the treatment of diabetes by insulin is mainly this that those diabetics who can remain glycosuric maintaining a normal blood sugar level and living a comfortable life by a quantitative restriction of diet alone do not ordinarily require insulin but those who cannot avoid glycosuria and hyperglycaemia on the maintenance diet (described in the previous chapter) do need it.

It has been stated before that the ideal aim in the treatment of diabetes mellitus is to keep the fasting level of blood sugar within normal limits. The urine may become sugar free but the blood sugar may still be 40 to 50 per cent

higher than normal. There are many practitioners who give insulin injections, taking the urinary sugar as the only guide. They usually stop the injections when the urine becomes sugar free, for fear of inducing hypoglycaemia, but the blood being still in the hyperglycaemic state, the pancreas does not get sufficient rest and so the ultimate result has often proved to be unsatisfactory. The ideal method of treatment would therefore, be to take as much strain out of the pancreas as practicable by trying to keep the blood sugar level as near normal as possible.

For helping practitioners in mofussil towns and villages to carry out insulin treatment by regular blood sugar tests, the author has devised a simplified method for the estimation of sugar in the blood the details of which are given in Chapter XIV.

Insulin treatment without regular blood sugar tests

When one has to depend upon the urinary sugar as the sole guide the following procedure may be found useful.

Calculate a diet for the patient according to his weight following the instructions given in the previous chapter. Divide this diet into 3 or 4 meals. Estimate how much sugar the patient passes 3 hours after each meal.

On the first day of treatment with insulin give a small dose 15 to 30 minutes before breakfast and see how far the urinary sugar goes down especially in the two specimens 3 hours after breakfast and 3 hours after dinner. If the sugar falls after breakfast but remains the same after dinner it shows that either the dose of insulin was insufficient or its effect did not last long. In that case, the dose of insulin should be increased say by 4 units. Now, if by increasing the dose of insulin the specimen after breakfast becomes sugar free but the specimen after dinner still contains sugar the dose should be kept constant for the next two days in order to see if the evening urine becomes ultimately sugar free. If it does not, there are two alternatives the first being to slightly increase the dose of insulin still further and the other being to give a second injection of a small dose of insulin in the afternoon say before tea.

When in this way the urine becomes free from sugar during the whole day for three or four days running, the carbohydrate in the diet may be increased concurrently with the dose of insulin till the required quantity of food sufficient for ordinary work is reached. Thus by care

Insulin is a complex protein derivative probably of the nature of a proteose and as such is likely to cause urticarial forms of allergy specially in diabetic patients who according to many workers have a peculiar predisposition to such reactions.

It appears that improvement in the mode of preparation of insulin has to some extent helped to lessen the allergic manifestations but in the more hypersensitive diabetic patients even crystalline insulin has been found to bring on undesirable and sometimes well marked anaphylactic reactions.

It is a significant fact however that diabetic patients who are extremely sensitive to one brand or preparation of insulin often become much less so when the brand is changed. Such a simple measure in such apparently grave crisis must be considered as a circumstance of great favour to most diabetic patients as otherwise one would either have to give up insulin treatment or do it at great risk and discomfort to the patient. Grave forms of insulin allergy severe enough to embarrass insulin therapy are rare.

Symptoms of insulin anaphylaxis—The symptoms of insulin anaphylaxis usually encountered begin as a rule within a short time of the injection sometimes within five minutes. A small or fur sized welt usually appears at the site of the injection followed almost immediately by urticarial rashes throughout the body. This causes an uncontrollable generalized itching which lasts for an hour or more. Grave constitutional symptoms such as nausea vomiting cardiac distress (as encountered in one case) have been fortunately rare among other cases under the author's observation.

Method of Desensitization—The usual method is to begin with an intradermal injection of a minute dose of diluted insulin followed by gradually increasing doses given at different intervals. If however allergic reactions appear the dose should be reduced and a start should be

made from the dose previous to the one which caused the reaction. Soluble crystalline insulin should preferably be used.

The procedure followed by the author is as follows — Give an initial dose of 0.001 ($\frac{1}{1000}$) units of insulin intradermally and follow it up with another three injections of 0.002 ($\frac{1}{500}$) units, 0.004 ($\frac{1}{250}$) units and 0.008 ($\frac{1}{125}$) units of insulin in the course of the day. If no reaction occurs on the first day dosages of 0.01 ($\frac{1}{100}$) units, 0.02 ($\frac{1}{50}$), 0.04 ($\frac{1}{25}$), 0.1 ($\frac{1}{10}$) units should be given the next day. If still no reactions occur dosages of 0.2, 0.5, 1 and 2 units should be given on the third day. The dose should then be gradually increased. In a certain number of cases the author has tried 8 injections all in the course of one day with no untoward event and with good results.

Dilution of insulin for purposes of desensitization — 5 units of crystalline insulin should be diluted with 50 cc of sterile normal saline. Each cc of this diluted solution will thus contain 0.1 unit of insulin. Mix 1 cc of this diluted insulin solution with 9 cc of sterile normal saline. 0.1 cc of this solution will thus contain 0.001 or ($\frac{1}{1000}$) units of insulin.

Desensitization with Histamine — Repeated injections of small doses of histamine phosphate also cause a progressive decrease in the insulin allergic reactions.

The new synthetic antihistamine drug Benadryl has also been used in cases of insulin allergy in the Mayo clinic with encouraging results.

Insulin Resistance

It is an usual finding that cases of diabetes on similar diet scales require more or less an uniform amount of insulin to keep them under control. This however is not true in all cases in some larger doses have to be given and

even then the ultimate results are not satisfactory. These latter cases are usually termed resistant or refractory cases. The opinion of the author however is that if a proper and careful adjustment of the diet and the dosage of insulin is made in these cases they usually react favourably though they may require larger dosages temporarily. The causes for the temporary higher requirement of the amount of insulin according to the author are usually sepsis nervous excitement and excessive worry which should be removed as far as possible.

Indications for insulin treatment

(1) Obviously in all cases of true diabetes mellitus where there is pronounced hyperglycæmia or marked glycosuria (with or without ketosis) the symptoms are usually so marked that no difficulty is experienced in coming to the conclusion that insulin treatment is indicated.

(2) In all cases of diabetes mellitus with complications such as coma tuberculosis infections etc insulin is indicated.

(3) Cases of pronounced diabetes mellitus in children or young men below 35 call for insulin treatment.

(4) Mild cases of diabetes mellitus with vague symptoms attributable to diabetes where a careful dietetic regime has failed to remove glycosuria or reduce hyperglycæmia say below 0.14 per cent also point to insulin treatment. If these cases are neglected on the ground of the vagueness of symptoms they are likely to develop definite symptoms or lead to complications later on such as (1) neuritis (2) carbuncles cellulitis gangrene etc (3) blindness (4) tuberculosis.

Dosage of insulin

It should be stated at the very outset that unlike most drugs insulin has no fixed dosages and that there is no hard and fast rule regarding the same. The dose may vary

in different cases according to the severity of the disease, the complications, the diet prescribed and various other factors. The author is able to cite many instances where insulin was wrongly and unwisely discarded owing to the use of improper or inadequate dosage. Those very cases on proper adjustment of the dose gave very good results. It is essential therefore that the correct dose of insulin should be worked out in every case individually.

The amount of glucose utilized per unit of insulin is different in different cases and even varies under changing conditions in the same case. It has however been roughly estimated that one unit of insulin usually causes 1 to 2 grammes of carbohydrates to be utilized in a moderately severe case of diabetes. In a milder case the carbohydrate utilization per unit of insulin is somewhat greater than this. This fact should be taken into consideration in selecting the proper dose for a given patient. As a method of ready reckoning it may be stated that the total amount of available glucose calculated from the patient's diet minus the total amount of glucose passed in the urine will roughly indicate the carbohydrate tolerance of the patient and the amount of glucose which is over the limit of tolerance (i.e. the amount excreted in the urine) must be covered by an adequate dose of insulin calculated according to the method given below.

Rough and ready method of calculating insulin dosage

Calculate the glucose value of the patient's diet according to the instructions already given on page 96. Calculate the total sugar excretion in grammes in 24 hours.

$$\begin{array}{l}
 \text{Total glucose value in diet } 194 \text{ gms.} \\
 \text{Total sugar excretion} \\
 \text{Total quantity of 24 hour urine } 1500 \text{ c.c. (150 oz.)} \\
 \text{Glucose present } 4 \\
 \text{Total sugar excretion (24 hours) } \frac{1500 \times 4}{100} = 60 \text{ gms.}
 \end{array}$$

194 - 60 = 134 grammes will therefore roughly indicate the tolerance of the patient.

The 60 grammes of glucose which is over the limit of the patient's tolerance will have to be covered by insulin injections in the ratio of 1 unit of insulin for every 2 grammes of glucose as mentioned before.

The dose of insulin to be injected will thus roughly be $\frac{60}{2} = 30$ units.

If however the calculated dose of insulin required much exceeds this dose it is safer to divide the dose into 2 larger and smaller fractions and give it in two injections instead of one. The larger dose should be given 20 minutes to half an hour before breakfast and the smaller dose given 8 hours later i.e. before tea.

If the case is more severe and requires much bigger doses gradual and cautious increase in the dosages has to be made.

It should be pointed out however that as already stated the method given above is only intended to be a rough and ready guide as to the approximate dose of insulin required for a given patient. The degree of fasting hyperglycemia present must always be taken into account and suitable adjustments of the insulin dosages made accordingly whenever necessary.

In some of the very severe cases requiring very big doses of insulin the injection has sometimes to be given more than twice daily and even then it has been found difficult to maintain a steady level of blood sugar near about the normal range throughout 24 hours. In such cases the use of the new insulin compound Protamine Zinc Insulin has often been found to be of great advantage and in some cases it has been found possible to keep even severe diabetics in good health even with one injection a day. The details are described in a previous chapter (Chapter II).

Insulin Mixture—It has already been stated that the action of protamine zinc insulin is very slow and gradual and if an injection is given before breakfast as is usually done it would not be able to effectively control the post

breakfast hyperglycaemia and glycosuria in a moderately severe case of diabetes. For the same reason it does not also effectively control the rapidly increasing hyperglycaemia following a high carbohydrate diet or in cases of severity with complications such as acidosis etc. In such cases a mixture of soluble insulin (for the quick control of the post breakfast hyperglycaemia) and protamine zinc insulin (for its slow and prolonged action) is advocated and is found to be of great advantage in effectively controlling the hyperglycaemia in severe cases of diabetes. No hard and fast rule can however be laid down as regards the proportion and the dosage of each of the two kinds of insulin to be used as much would naturally depend on the individual cases and has to be varied even in the same case according to the results obtained.

As a practical measure it may be noted that in drawing the two insulin solutions in the same syringe the soluble insulin should be drawn in the syringe first and then the requisite amount of protamine zinc insulin drawn and mixed in the syringe. If the process is reversed i.e. if the buffered protamine zinc insulin is drawn first there is risk of inactivation of the real soluble insulin if any protamine zinc insulin be introduced into the phial.

Contraindications for insulin treatment

(1) All cases of renal glycosuria or glycosuria of non diabetic origin. Very careful diagnosis by the methods suggested before should be made.

(2) Certain cardiac diseases. It sometimes requires very careful judgment on the part of the physician to decide in cases of diabetes complicated with cardiac diseases whether to give insulin or not.

The experience of the author goes to show that insulin may prove to be very dangerous in cases of marked myocardial degeneration and in angina pectoris. Before deciding to give insulin to any patient it is the duty of the physician

to examine the heart carefully and to enquire if the patient has suffered from anginal attacks

In such cases where it is found that insulin treatment is the only chance of saving the life of the patient the physician has to go very carefully and feel his way at every step. One of the main points which he should bear in mind is that he should never attempt to make the patient sugar free. If hypoglycæmia develops in these cases it may prove fatal.

It may however be stated that ordinary valvular diseases of the heart may be treated with insulin with a fair margin of safety but the physician must also try to prevent hypoglycæmia as far as possible.

A few general hints on insulin treatment

(1) Always aim at keeping the blood sugar level as near the normal limit as possible

(2) The selection of the proper dose and the spacing of insulin injections are the difficult parts of the treatment. Too small a dose or one given at too long an interval often does not produce the desired effect. A dose too big or given too soon after the first injection often produces nasty reactions.

(3) There must be a definite and close relationship between the dose of insulin and the sugar value of the diet given according to the tolerance of the patient.

(4) The decrease of hyperglycæmia and glycosuria should be carefully noted at every step and the dose of insulin regulated accordingly.

(5) Injections of soluble insulin should preferably be given fifteen minutes or half an hour before meals. Injections of Protamine Zinc insulin may be given 45 minutes to one hour before meals.

(6) All forms of hard or strenuous exercises should be strictly forbidden for at least 3 or 4 hours after insulin injection.

(7) Even a minor infection upsets the sugar tolerance of the diabetic patient. This should be remembered and an increase in the usual dose should be made if the patient suddenly develops such an infection. In major infections much increase in the dose is necessary. In patients suffering from acute infections such as tonsillitis, bronchitis or pneumonia always guard against acidosis by proper adjustment of the diet and the dose of insulin.

(8) If possible all cases of diabetes undergoing surgical operation urgent or non urgent should be made sugar and ketone free and the blood sugar brought down to normal.

(9) In diabetic pregnant women sudden variations in sugar tolerance may take place leading to severe acidosis. Insulin treatment should be commenced on the slightest indication of acidosis.

(10) It should be remembered that in diabetes complicated with tuberculosis of the lungs insulin plays an important part because with its aid a satisfactory diet which is essential to maintain the resistance and the body weight of the patient can be given.

(11) Insulin has also been found to be of help in the treatment of a few cases of acidosis of non diabetic origin such as hyperemesis gravidarum and surgical shock of non diabetic individuals. In these cases sufficient glucose must be given to the patient after insulin injection to prevent any chance of hypoglycemia.

(12) Small doses of insulin followed by glucose has also been found to be useful in a few cases of malnutrition sprue etc.

Vitamins in Diabetes

Vitamin B₁

Thiamin chloride ($C_8H_{13}N_4SOCl \cdot HCl$)

Water soluble and partially thermolabile

Sources—Germ and pericarp of cereals enriched bread yeasts and legume seeds, yolk of eggs liver, meat particularly pork certain fruits and vegetables

Vitamin B₁ is relatively resistant to heat but is destroyed by prolonged boiling

Action on carbohydrate metabolism—It has definitely been shown that in thiamin deficiency the carbohydrate tolerance is definitely lowered. Thiamin catalyzes the transformation of pyruvic acid (an intermediate product in the oxidation of carbohydrates) and thus helps the carbohydrate metabolism. Deficiency of thiamin therefore interferes with the normal metabolic interplay between glycogen lactic and pyruvic acid. In normal carbohydrate metabolism thiamin is believed to act as a coenzyme and helps in the enzymic activation of the oxidation of pyruvic acid and hence in thiamin deficiency the carbohydrate metabolism stops with the formation of pyruvic acid which thus accumulates in the blood.

Action in diabetes—The role of vitamin B₁ in human diabetes has been a subject of controversy for some time past. The author has been engaged in this study for some years and from the results of the experiments hitherto obtained he is in a position to say that in a good number of these cases a definite improvement in the carbohydrate metabolism frequently follows an intensive vitamin B₁ therapy along with an improvement in the general condition of the patient. The improvement or otherwise of a diabetic patient as a consequence of vitamin B₁ therapy of course depends on whether there is vitamin B₁ deficiency or not. The symptoms of thiamin deficiency are rather vague but the main specific symptoms were anorexia gastro-intestinal hypotonia, constipation indefinite pains paraesthesia etc.

In cases of thiamin deficiency a marked improvement in the general health of the patient quickly occurs as a result of vitamin B₁ therapy.

Vitamin C

Ascorbic or Cevitamic acid ($C_6H_8O_6$)

Water soluble and heat labile

Sources—Fresh fruits and vegetables particularly lemons, pumelo (Birabi lebu) and other citrous fruits tomatoes etc. non-pasteurized cow's milk etc.

Action on Diabetes—It has been shown that in uncomplicated cases of diabetes whose vitamin C intake has been adequate the fasting level of plasma ascorbic acid is normal. The administration of ascorbic acid in these cases had no effect on the progress of the disease. Most observers do not support the idea of any specific relationship of vitamin C to diabetes.

The author studied the effect of ascorbic acid in diabetic patients of various grades of severity and is of opinion that administration of vitamin C even in large doses does not affect the severity of the diabetic condition.

In recent studies on experimental diabetes caused by Alloxan it has also been proved that injections of ascorbic acid did not protect animals against Alloxan and did not in any way deflect the course of Alloxan diabetes.

CHAPTER XI

SOME OF THE DANGERS AND COMPLICATIONS OF DIABETES AND THEIR TREATMENT

The most serious dangers which threaten a diabetic patient are coma, gangrene, carbuncles, acute infection, severe nephritis, tuberculosis, etc.

Diabetic acidosis and Coma—We know that in diabetes not only the carbohydrate metabolism but also that of protein and fat are affected. We also know that normal carbohydrate combustion in the system is always accompanied by a defective fat metabolism, because, as has been stated before, "fat in the food burns in the flame of carbohydrates" and that without it "the fire smokes".

For the proper utilization of fat, the simultaneous oxidation of a definite amount of carbohydrate is essential and if the system is unable to burn the requisite amount of glucose, a portion of the fat is incompletely oxidized as a result ketone bodies are formed and accumulate in the blood. The system tries to get rid of this excess ketone production in two ways —

- (1) By excretion in the urine as free acid, and
- (2) By neutralization of the acid bodies and excretion of the resultant bases in the urine.

When the production of the acid bodies is excessive the neutralization is effected by withdrawal of fixed bases, chiefly, sodium and potassium, from the blood and tissues. This naturally results in the depletion of the alkali reserve and in a reduction in the bases of the blood. A low concentration, not only of the total salts, but also of the total electrolyte in the body fluid thus results.

The excretion of large amounts of fluids, in the attempt to remove these acid bodies from the blood, naturally results in dehydration and haemo-concentration, as well as a severe

depletion of the bases and of the chloride content. The alkali reserve of the body is also depleted for the same reason resulting in the reduction of the carbon dioxide combining power of the plasma.

Causes of Diabetic Coma

The usual causes of severe acidosis and coma are (1) sudden dietetic unbalance (2) sudden stoppage of insulin and (3) infections. These are often preventable and every patient should be pre warned against them. They should particularly be warned against the dangers of neglecting an infection of any kind however slight it may apparently appear to be at the beginning. It should always be remembered that infection aggravates the diabetic condition suddenly and often precipitates coma.

Diagnosis—The diagnosis of severe acidosis and diabetic coma may often be made clinically with a fair degree of accuracy if the patient is known to be a diabetic. Among the characteristic points in the bedside diagnosis of diabetic acidosis and coma the following may be noted —

- (1) Headache drowsiness or actual coma
- (2) Anorexia vomiting abdominal pain
- (3) Skin—very dry due to severe dehydration
- (4) Respiration—Characteristic deep and slow abdominal type of breathing (air hunger)
- (5) Eyes—Low tension of the eye balls. This is a very characteristic sign and is often diagnostic
- (6) Pulse—low tension and a high rate
- (7) Blood pressure—low
- (8) Breath—Characteristic aromatic (acetone) odour

Among the chief laboratory findings of importance in a case of diabetic acidosis and coma the following are of importance and should be ascertained whenever possible —

Blood

Blood sugar—This is invariably very high but there seems to be no definite relationship between the degree of

hyperglycemia and the depth of the coma. In one of the author's cases with a blood sugar of 1.08 per cent (1080 mgs) the patient could still be roused and he recovered ultimately.

Leucocytosis—This is usually present and may be very high in some cases.

Serum potassium concentration—According to recent observations by the author it appears that the maintenance of normal concentration of the serum potassium has a very important bearing on the prognosis of severe diabetic acidosis and coma. A progressive lowering in the concentration of serum potassium has been observed in some cases of diabetic coma and this may cause death if the depletion is severe in spite of the blood sugar level and the plasma CO₂ being more or less within normal limits.

A severe depletion of serum potassium is usually indicated by marked respiratory difficulty, difficulty in swallowing and extreme muscular prostration.

Carbon dioxide combining power of the plasma (alkali reserve)—In healthy individuals the plasma (at rest) contains 55 to 70 cc of CO₂ (bound as bi-carbonate) per 100 cc of plasma measured at 0°C and 760 mm pressure. In bad cases of diabetic acidosis this figure is much less (below 40 volumes per cent) and in severe cases it may go down to 20 volumes or even less. This test is usually done by the Van Slyke method.

Carbon dioxide in alveolar air—Normally the carbon dioxide content in the alveolar air is about 5 per cent but may fall to 2 per cent or below in cases of diabetic coma. The possibility of doing this test at the bed side is a further advantage of this method. This is usually done by Friedlander's method and is fairly simple.

Urine—The urine besides containing huge amounts of sugar invariably contains fair and huge amounts of ketone bodies. The determination of the total acidity of the urine

and the ammonia coefficient (i.e., the relation between the urinary ammonia and the total nitrogen) often gives useful information particularly in adjudging the effect of the treatment.

Differential Diagnosis—When however a patient is seen for the first time in an unconscious state and when the previous history of the case is unknown or not available it may often present difficulties in making a diagnosis of diabetic coma on the spot because the physician has to bear in mind some of the other causes of unconsciousness the noteworthy amongst them being hypoglycæmic coma, uremic, cerebral hemorrhage and meningitis. The following distinctive clinical features in each of the above individual conditions will however help in making the differential diagnosis easier.

Hypoglycæmic Coma—

- Onset—sudden
- Respiration—shallow
- Pulse—often irregular
- Skin—moist
- Eyes—tension normal Double vision at times
- Pupils—present
- Blood pressure—normal
- Blood sugar—low
- Urine sugar and ketones—usually absent

Uremic Coma

- Onset—slow
- Respiration—cheyne stokes type
- Pulse—full and bounding
- Skin—dry
- Eyes—high tension of the eye balls
- Muscular twitchings
- Blood pressure—usually high
- Urine—albumin casts RBC etc

hyperglycemia and the depth of the coma. In one of author's cases with a blood sugar of 1.08 per cent (1 mgs) the patient could still be roused and he recovered ultimately.

Leucocytosis—This is usually present and may be very high in some cases.

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Carbon dioxide in alveolar air—Normally the carbon dioxide content in the alveolar air is about 5 per cent but may fall to 2 per cent or below in cases of diabetic coma. The possibility of doing this test at the bed side is a further advantage of this method. This is usually done by Friedlander's method and is fairly simple.

Urine—The urine besides containing large amounts of sugar invariably contains fat and large amounts of ketone bodies. The determination of the total acidity of the urine

and the ammonia coefficient (i.e. the relation between the urinary ammonia and the total nitrogen) often gives useful information particularly in judging the effect of the treatment.

Differential Diagnosis—When however a patient is seen for the first time in an unconscious state and when the previous history of the case is unknown or not available it may often present difficulties in making a diagnosis of diabetic coma on the spot because the physician has to bear in mind some of the other causes of unconsciousness the noteworthy amongst them being hypoglycaemic coma, anaemia, cerebral haemorrhage and meningitis. The following distinctive clinical features in each of the above individual conditions will however help in making the differential diagnosis easier.

Hypoglycaemic Coma—

- Onset—sudden
- Respiration—shallow
- Pulse—often irregular
- Skin—moist
- Eyes—tension normal Double vision at times
- Tremor—present
- Blood pressure—normal
- Blood sugar—low
- Urine sugar and ketones—usually absent

Uraemic Coma—

- Onset—slow
- Respiration—Cheyne Stokes type
- Pulse—full and bounding
- Skin—dry
- Eyes—high tension of the eye balls
- Muscular twitchings
- Blood pressure—usually high
- Urine—albumin casts R B C etc

Cerebral hæmorrhage—

Onset—rapid

Respiration—stertorous usually foam-covered lips

Eyes—pupils dilated and unequal conjugate deviation

Unequal resistance of limbs in lifting

Blood pressure—high

*Glycosuria may be present**Meningitis—*

Onset—sudden

Respiration—rapid

Eyes—pupils dilated or unequal

Fever—present

Leucocytosis

Kerning's sign

Glycosuria may be present

It is thus essential that before starting vigorous treatment proper diagnosis should carefully be made

Treatment —It should be fully realized that a true case of diabetic coma is as much an emergency as a case of acute appendicitis or a spreading peritonitis and the treatment should be prompt vigorous and thorough. In the pre insulin days the outlook for these cases was very gloomy indeed almost every case proving fatal even with the best possible help but with the advent of insulin there has been a complete change for the better so much so that with an early administration of insulin in suitable doses the recoveries are so frequent that they are no longer considered even worthy of record.

The following main principles must be borne in mind in the treatment of a case of diabetic coma —

(1) That the cause of the ketosis (which leads to coma) is disordered fat metabolism which in its turn is due to defective sugar combustion and that if sufficient sugar can

be made to burn in the system the ketosis will disappear. Thus the importance of giving insulin *early* and in *proper* doses according to the severity of the case is at once made manifest. It should be noted that to give small doses of insulin in cases of true coma where much bigger doses are required is playing with the life of the patient and if the general practitioner who is called upon to see the case has no special experience or aptitude in the treatment of such cases he should give the patient a large dose of insulin with glucose and send him to hospital at once.

(2) That the coma is often precipitated by an acute infection of some kind often causing profound toxæmia. The septic focus should be determined and the source of the toxæmia should be eliminated if possible. Insulin is relatively ineffective in the presence of a severe toxæmia.

(3) That in some bad cases of diabetic coma there is severe dehydration which is sometimes so marked as to cause a shrunken appearance of the patient simulating a case of cholera. This is due to severe loss of fluid owing to previous polyuria and vomiting and sometimes causes a marked fall in the blood pressure, low tension in the eye balls, a feeble and thready pulse and a circulatory collapse and unless this condition is promptly treated by administering large quantities of fluid (intravenous or subcutaneous saline as the case may require) the patient dies of circulatory collapse from which insulin alone is unable to save him.

(4) That the strain on the heart in patients suffering from diabetic coma is often considerable—the strain involved in hyperpnoea alone being much too high and the heart experiences great difficulty in withstanding the demands made on it. Every precaution must therefore be taken to protect the heart.

Main points in the treatment of diabetic coma—

- (1) *Care*—keep the patient warm in charge of a trained nurse if possible.

- (2) *Insulin*—Give insulin (soluble) immediately on diagnosis in adequate doses and repeat at intervals of 3 hours (or earlier in extreme cases) till there is clinical or laboratory evidence of improvement
- (3) *Fluids*—Treat dehydration energetically by adequate administration of fluids. It should be remembered that this procedure is as important as administration of insulin
- (4) *Gastric Lavage*—Remove gastric contents by a gentle lavage with warm normal saline. This procedure checks vomiting, prevents abdominal distension and often relieves cardiac distress
- (5) *Enema*—Relieve a distended rectum by enema
- (6) *Circulatory stimulants*—In threatened circulatory collapse give Epinephrine in 0.5 to 1 cc doses. Ephedrine may be given in 25 to 50 mg doses if the blood pressure is rapidly falling. Treat other conditions according to circumstances
- (7) *Blood sugar*—Do blood sugar tests as frequently as practicable to regulate insulin dosage
- (8) *Blood pressure*—This should be taken frequently. Systolic pressure below 100 mm usually means bad prognosis
- (9) *Glucose*—Vide infra
- (10) *All allies*—Vide infra
- (11) *Septic Foci*—The septic focus if any should be sought for and removed as much as possible

The Position of Glucose Therapy in the Treatment of Diabetic Acidosis and Coma

Before going into the details of treatment a few words should be said regarding the real position of glucose therapy

in the treatment of diabetic coma about which a good deal of controversy still exists. Taking the extreme views on the subject we have Hinworth* on the one hand who believes that the essential therapeutic agent in the treatment of diabetic intoxication is glucose—the fundamental idea being to give glucose glucose *always* covered by the necessary amount of insulin—and not insulin covered if necessary by glucose as is the current practice. Joslin† on the other hand holds the opposite view. According to him there is no need of protecting the patient against insulin by the administration of glucose. It is better to concentrate on protecting the patient with insulin by watching changes in the blood and the urine sugars in order that the proper amount of insulin may be given.

According to some authorities the method of procedure in the treatment of diabetic coma is the initial administration of insulin without glucose because they argue that with the surplus sugar circulating in the blood the giving of extra glucose is unnecessary. There are many others however who are definitely of opinion that glucose should always be given along with the insulin injection because they argue that it is better to allow the hyperglycemia to go on than to produce hypoglycemia which is sometimes a dangerous complication in diabetic coma difficult to detect immediately.

Without going into the details of the controversy the author is definitely of opinion that it is certainly a wiser policy to give glucose in suitable doses along with insulin injections. One of the great advantages of this method of treatment is that by following this plan the average practitioner feels safer in giving large doses of insulin which is the one thing absolutely essential for the patient's recovery from coma. Besides when the ketosis is of a grave and perilous nature the extra amount of glucose given will permit of heroic doses of insulin being administered. This

* *Lancet* CCXXXI 185

† *Med. Clin. North Amer.* 22 829 1927

will ensure the prompt oxidation of a large amount of glucose in circulation and the improvement in the fat combustion thus effected will cause simultaneous and rapid reduction in the ketone bodies. Against the argument that an unnecessary production of hyperglycæmia is caused through administration of glucose it may be said that it has been shown by experiments that a prolongation of hyperglycæmia does not in any way affect the recovery of the patient from diabetic coma if sufficient insulin is given to oxidize it. Coma has been found to clear up even though hyperglycæmia is still present. In one of the author's cases the patient had an uneventful recovery from coma even with a blood sugar of over 1 per cent. The only point to remember is that the total amount of glucose administered must have a definite relationship to the total daily dose of insulin given and if glucose is given intravenously its strength should rarely exceed 10 per cent.

Treatment of pre-comatose conditions—Here: though the patient is usually very drowsy he can still be roused and made to swallow. Circulatory collapse due to dehydration is usually less frequent and these cases are more easy to deal with.

The general principles of treatment follow the lines outlined above.

The bowels should be cleared and if there is vomiting a stomach wash should be given with a warm sodium bicarbonate solution (3ii to one pint).

10 to 60 units of insulin should be given immediately followed by about 40 grammes of glucose by mouth either as glucose solution flavoured with lemon juice or in the shape of orange juice—(about 16 ounces of the juice) plenty of fluids should be given in the shape of water tea barley water and alkaline drinks. The urine should be collected 2 hours after the injection and examined for sugar acetone and diacetic acid and if possible a sample of blood should be collected for estimation of blood sugar. If the

blood sugar is still very high and the urine contains a fair amount of sugar acetone and diacetic acid a similar dose of insulin should be given followed by some more glucose. The dose of insulin will in this way have to be regulated very cautiously according to the improvement or otherwise in the patient's condition verified by urine and blood sugar tests. As the condition improves the dose of insulin will have to be decreased and the interval between the injections increased till the blood sugar comes down to below say 0.2 per cent and the acetone bodies disappear from the urine. It is a wise thing not to allow the urine to become completely sugar free till the patient can be declared to be out of danger. This is easily possible by a judicious adjustment of the dose the interval of insulin injections and the amount of sugar given to the patient. It is unnecessary to add that the patient must be on a liquid diet chiefly consisting of carbohydrates.

Treatment of complete coma—Though the main principles of the treatment are the same these cases present many difficulties owing to the number of complications present. In these cases the patient is absolutely unconscious and hence cannot swallow. Besides in some of the very severe cases there is usually marked dehydration and severe cardio-vascular collapse. Treatment in such conditions requires much tact care and promptness on the part of the physician because insulin alone or insulin and glucose combined may fail to bring the patient round and unless prompt and energetic measures are properly taken these patients may die of circulatory failure in spite of having big doses of insulin. To prevent circulatory collapse enough of fluids should be promptly given to replace the fluid lost in the tissues. As a matter of fact the treatment of these cases should be more or less on the same lines as in cholera viz introduction of saline by the intravenous subcutaneous and the rectal route.

The exact strength of the saline to be used for this purpose is a matter of opinion. Some prefer hypertonic

saline solution for the first infusion, others use normal solution. The author prefers to use the latter but combines glucose with this, so that the strength of the glucose in the solution becomes 10 per cent, as in the following formula —

Glucose (pure anhydrous)	60 grammes
Sodi chlor (pure)	5 "
Aqua	1 pint

The proportion of glucose in the above solution will be 8 grammes per ounce. The glucose used in the preparation of this solution should be extra pure, of the anhydrous variety, specially used for intravenous injections, and should be properly sterilized.

About $1\frac{1}{2}$ pints of this solution containing about 90 grammes of glucose should be given by the intravenous route very slowly. At least one hour should be taken to give the intravenous injection and the temperature of the fluid should be about 106°F . Fifty units of insulin should be given subcutaneously or intravenously at the commencement of the intravenous glucose saline injection and another 40 units when half of the solution has been injected. Some authorities prefer to give 7 per cent gum acacia solution in addition the idea being that it remains in the circulation better than the glucose saline alone. Glucose and saline may also be given per rectum.

If necessary, the above treatment may be repeated after 3 hours—the amount of fluid to be injected, the dose of insulin, etc., depending on the patient's condition and on the result of blood and urine tests.

When, in this way, the patient recovers from coma—the dehydration becoming less marked and the patient being able to swallow—the fluid introduced intravenously should be regulated or stopped and the patient should be given glucose by the mouth. The dose of insulin and the amount of glucose will of course have to be regulated

according to the condition of the patient till the patient sufficiently recovers and the acetone bodies disappear from the urine and remain absent on repeated examinations. The patient may then be put on a gradually increasing diet chiefly consisting of carbohydrates. The dose of insulin and the interval between the injections should also be accordingly regulated.

Alkalies and Diabetic Acidosis

The use of alkalies in large doses used to be the standard treatment of acidosis and diabetic coma but at the present time there is diversity of opinion regarding the value of alkalies in such conditions. An authority of the eminence of Joslin takes the view that alkalies in such cases are useless if not harmful. His reasons may be summarized as follows —

(1) Groups of cases treated without alkalies give very much more satisfactory results than the group treated with alkalies.

(2) When the alkalinity of the blood of a patient is brought back to normal coma may still persist.

(3) Alkalies are liable to upset the stomach which is not desirable in diabetic coma.

(4) Large doses of alkalies in a few bad cases have led to convulsions.

Haldane demonstrated some time ago that if large doses of sodium bicarbonate were given to normal subjects receiving normal diet the tolerance for glucose was depressed and acetone bodies appeared in the urine.

Harrison and his co-workers have shown that sodium lactate may be substituted for sodium bi-carbonate with gratifying clinical results. The conversion of sodi lactate to sodi bicarb is gradual and hence there is less likelihood of the development of alkalosis. Besides sodium lactate solution is non-irritating, stable and can be sterilized by boiling.

In cases of amputations of the limbs the use of ice refrigeration anaesthesia appears to have gained considerable ground recently. The advantages of this method appear to be that it prevents shock, preserves tissue vitality and eliminates post operative oedema.

Acute Infective Condition in Diabetes

It has already been stated that an infection aggravates the diabetic condition and frequently brings on acidosis and coma. It should further be remembered that unless the infective processes can be arrested the acidosis resulting from surgical infections goes on increasing and becomes very much resistant to treatment.

Recent advances in the treatment of infective processes in diabetes have however brought down the mortality rate considerably. Speedy healing of the tissues is insured by control of the hyperglycaemia with insulin and the use of penicillin and the sulfonamide group of drugs has very considerably helped in bringing about quick arrest of the spread of the infective process.

Penicillin therapy—It must be admitted at the outset that the recent introduction of penicillin has brought about a marked advance and a revolution in the treatment of certain infective processes in diabetes, particularly carbuncles and cellulitis. It has doubtless completely changed the outlook and the prognosis of these cases and if used early enough and in fairly big doses (500,000 units or more per day) the spread of the infection is arrested almost immediately and a subsidence of the process takes place without the necessity of any surgical interference. It has undoubtedly reduced the mortality rate and is doubtless a great boon to the diabetics.

Sulfonamide therapy—Drugs of this group viz., sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine may also be used as successfully in diabetes as in nondiabetics.

Sulfadiazine may however be considered to be the drug of choice in most infections

Furunculosis

Extensive furunculosis in diabetes is dangerous not only because the diabetic has usually a poor resistance to infections but also because it is liable to aggravate even a mild case of diabetes to a serious degree. It is therefore very important to test the urine and the blood sugar early and frequently in all cases of boils and furuncles.

The treatment of diabetic boils and furuncles has been dealt with later in connection with the diseases of the skin.

Carbuncles

This is a fairly common complication and is not infrequently a fatal one for reasons already explained. It should be remembered that the acidosis resulting from surgical infection is very much more resistant to treatment than a straightforward case of diabetic coma and the prognosis is often bad.

Treatment

General—It is important to have the patient confined to bed from the very beginning. All the general measures mentioned before should be scrupulously carried out.

Penicillin therapy—This should be resorted to as early as possible in doses of 50 000 to 100 000 units every 3 or 4 hours depending on the seriousness of the infection and the response obtained. A marvellous result has often been obtained if the therapy is started early.

The use of sulfonamide group of drugs more particularly sulfadiazine is also advocated when necessary if the usual care is taken to watch for leucopenia, anemia and hematuria as in the case of non diabetics.

Local treatment—One of the most efficient local applications is magnesium sulphate paste* according to the following formula —

R/

Dessicated magnesium sulphate	12 ounces
Acid carbohc (pure)	$\frac{1}{2}$ drachm
Glycerine (pure)	6 ounces

This should be applied over the rough surface on a piece of sterile lint and changed morning and evening

Surgical treatment—With early diagnosis and energetic treatment, surgery is seldom required in the treatment of carbuncle. In neglected or spreading carbuncle with much slough formation, crucial incisions with under-cutting of the skin is a time honoured procedure. The wound may require packing for 24 hours after which period the magnesium sulphate paste may be used with benefit.

Auto hæmo therapy—In early cases this method of treatment has been found to be of use in limiting the extension of the carbuncle and in stimulation of the healing process.

Vaccines—Auto-vaccines have been recommended for augmenting the immunological reactions.

Circulatory Disorders and Gangrene

Diabetic Gangrene—If trauma and infections could be eliminated, death from diabetic gangrene would probably disappear. The prophylaxis for gangrene includes care of the foot and treatment of minor foot injuries and a very careful control of diabetes. A diabetic patient should pay more attention to his feet particularly his toe nails than his face. Many patients infect themselves when trimming their own nails. It is important to educate every diabetic on the care of his feet, specially with regard to the

* Heat magnesium sulphate to 100°C powder while hot and add glycerine and phenol gradually. Strength of phenol is about 1 per cent.

paring of corns and the dressing of blisters and the selection of the proper footwear*.

Diabetic gangrene usually occurs in persons over 40 years of age and often starts from a trivial injury to the part. The condition is usually associated with gross arterial disease and is in the nature of an arterio-sclerotic gangrene. The prognosis is grave and death may ensue from toxæmia or diabetic coma. Although insulin has robbed diabetes of many of its surgical complications, it cannot be expected to aid in limiting gangrene.

Treatment—Immediate attention to and control of the acute infective processes and the acidosis caused thereby have just been described and it is essential that these should be followed with the utmost care and patience. Vigorous anti-diabetic treatment should be undertaken at once and a serious attempt made to check the spread of the infective processes by suitable penicillin and sulfonamide therapy as has just been described.

Conservative measures to save as much of the limb as possible may be successful in early cases. The object of surgical treatment is to convert a moist gangrene into a dry one and this may be effected by means of strict asepsis, adequate splintage and suspension of the limb. Foot baths and irrigation are now employed less frequently. Local amputation may be performed after a line of demarcation has formed.

In serious cases with gross arterial disease conservative treatment with a view to saving the limb is not justified. Where life is endangered the limb must be sacrificed and an early amputation is imperative. The classical site of selection is above the knee joint and a high amputation may be performed under gas and oxygen anaesthesia. Spinal anaesthesia is an alternative method preferred by some surgeons.

* The shoes purchased should, for example, fit the feet a 1/2 of the eyes.

Diseases of the Skin and Diabetes

Diabetic patients show a higher incidence of certain skin diseases than other persons. It has been suggested that hyperglycemia acts as a chemical irritant to the skin and is a factor of importance in the etiology of certain diseases of the skin. Even in non diabetic subjects suffering from diseases of the skin the blood sugar has often been found to be above normal. In most of these cases there is also a simultaneous rise in the sugar content of the sweat* and of the skin†.

The skin may be considered to be one of the main store houses of glycogen the other two being the liver and the skeletal muscles. It is not sufficiently realized that the skin takes a very active part in converting the excess of sugar in the blood into glycogen and storing it as such. In severe diabetes the glycogen content of the skin is very deficient and is replaced to a large extent by unutilized sugar and thus the cutaneous sugar value in diabetes is considerably increased.

In diabetes the skin loses its power of converting the excess of sugar into glycogen the extent of which depends on the severity of the case. The glycogen content of the skin is thus gradually depleted and is replaced by the unutilized sugar and thus the sugar content of the skin increases sometimes considerably. The loss of power of glycogen formation the depletion of the glycogen content and the increase in the cutaneous sugar value take away much of the protective power of the skin and naturally makes it more vulnerable to infections. The skin becomes dry and deteriorates in quality and texture. It should always be kept in mind that the first step in the treatment of such condition should be the replacement of glycogen content of the skin by insulin.

* The average normal sugar content of sweat is 15 milligrammes per 100 c.c.

† The average normal sugar content of the skin is 65 milligrammes per 100 gm. of skin.

The following are some of the common varieties of skin affections met with in diabetes —

Allergy	Furunculosis
Carbuncle	Gangrene
Eczema	Impetigo
Pruritus	Pruritus
Tolerant	Xanthelasma

Of the above folliculitis, furunculosis, pruritus, carbuncle and gangrene appear to be the commonest.

Folliculitis and furunculosis—These are common complications of diabetes and are usually due to a deep staphylococcus infection.

Treatment—The treatment should be commenced early. If there is generalized folliculitis or furunculosis the whole body should be washed twice daily with a weak solution of potassium permanganate after which it should be wiped dry with a sterilized gauze without rubbing to avoid breaking open any pustule. The individual furuncles should be touched with 4 per cent alcoholic solution of gentian violet or a solution of triple dye containing acriflavin, brilliant green and gentian violet. Then the following dusting powder should be dabbed all over the body —

Sulphur	1/2 ounce
Canthar	1/2
Zinc oxide	4
Boric acid	3
Talc powder	1 ounce

It should be remembered that the linen worn next to the skin should be changed daily.

Vaccine or non specific protein therapy may be tried in resistant cases. Active anti-diabetic treatment should be undertaken.

Pruritus—This is also one of the common complications and may be generalized or more commonly localized specially in or about the private parts. The chief symptom

is an insatiable itching which is sometimes of such severity as to exclude the patient from society and to make him dull and morose. The denudation of the epithelial surfaces caused by ceaseless scratching makes it easy for the microorganisms and parasites to gain entrance to the affected part and complicate matters. The highly acid sugary urine also coming in contact with the part makes it still worse. This condition in male subjects is usually confined to the glans and the prepuce but may spread and produce a condition of balanoposthitis. It may also spread over the scrotum and perineum and the inner part of the thighs. The prepuce may be swollen and marked by radiating fissures.

In females the whole vulva may be affected the eruption spreading on to the skin of the perineum and the inner part of the thighs. The vaginal orifice may be swollen and excoriations and cracks may form. In chronic cases hypertrophy and lichenification may take place.

Treatment—The keynote of treatment is absolute cleanliness of the affected part use of simple lotions dusting powders or ointments as are found suitable and active anti-diabetic treatment the last named of course being more important. The use of a bland non-irritating oil to prevent irritation during micturition is often helpful. It should be remembered that one should not over-treat this condition. Simple cooling soothing liniments such as lint calamine (extra B. P.) sometimes give more relief than drastic methods of treatment.

If the itching is severe the part should be washed with a hot lysol lotion (15 drops of pure lysol to 1 pint of hot water) and after drying 2 per cent brilliant green or 1 per cent mercurochrome solution should be applied. Usually the condition clears up soon but if pruritus pudendi persists in spite of above treatment accompanied by severe anti-diabetic regime one should promptly search for a local cause which is usually prolapse leucorrhœa or urinary incontinence.

Prophylaxis—It is the physician's duty to tell every one of his diabetic patients to keep their skin absolutely clean. The patients should be warned about the complications which may follow if the hygiene of the skin is neglected. The simple cuts, the slightest blisters and the most trivial skin infections have been known to be followed by very serious consequences such as cellulitis and gangrene.

Xanthoma Diabeticorum

This is a rare complication in diabetes. A review of the literature on the subject would show that during the last 100 years the number of cases described would not exceed one hundred and fifty. During the last 25 years the author came across only two typical cases, the more recent case being that of a young boy of 20 years of age.* A description of the skin lesions in this case is given below—

Practically the whole body and the extremities were covered with small yellow-coloured papular lesions. The extensor surfaces of the limbs suffered more than other parts. The lesions present in the face were small discrete and confined mostly to the forehead. The lesions in the hands were found to be generally confined to the sides and the back of the fingers and in the webs between the fingers and somewhat simulated scabies. The palms of the hands and soles of the feet were sparsely affected. The individual lesions were yellow or orange-coloured flat topped papules varying in size from a pin head to that of a split pea. Most of these were solid but some were soft in consistency.

Histopathology—The epidermis was mostly affected. The main changes were confined to the corium. In the subpapillary layer the capillaries were dilated in the affected area and there were cellular infiltrations round the dilated capillaries and also throughout the corium.

* *Indo Med Gaz* Vol. 87 No. 11 1947

These cells consisted of endothelial cells round cells and epithelioid cells. There was all round fatty and fibrous degeneration in the corium the fatty degeneration being more marked than the fibrous changes. Throughout the whole corium were deposits of fat globules and granules both inside the degenerated cells and the intercellular spaces.

The case described above presented a few unusual features the most noteworthy being that though the hyperglycemia and the lipæmia particularly the latter were pronounced and though the skin lesions were wide spread the marked improvement in the clinical condition the quick disappearance of the hyperglycemia and lipæmia and a resolution of the skin lesions were almost dramatic.

Investigation—Among the noteworthy positive findings in the biochemical investigations* the hyperglycemia was fairly marked the cholesterol content of the blood was extremely high. As a matter of fact marked lipæmia was a special feature in the case. The urine was loaded with sugar (8 to 10 per cent. in 24 hours collection) and a fair degree of ketonuria was present.

Treatment—The patient was put on a very low fat diet and an intensive anti diabetic treatment given. Within a short period very satisfactory result was obtained and the skin condition improved considerably till it finally disappeared.

The author is inclined to be of opinion that Xanthoma diabeticorum is related more closely to fat metabolism of diabetes mellitus than to the disturbance of carbohydrate metabolism.

Bronzed Diabetes

Bronzed diabetes is a rare condition. It is characterized by three conditions *viz.* pigmentation of the skin and mucous membrane hepatic cirrhosis and diabetes.

* For det. ls. consult original paper

Neuritis and Neuralgias

These are fairly common complications. Diabetic neuralgia may affect all the nerves of the body but the common forms are the brachial sciatic and intercostal neuralgias. The neuralgias in diabetes are usually more painful than the ordinary forms. They may be symmetrical and do not yield to treatment readily. The author had a few cases where the pain persisted (to some extent) even after the blood sugar had come down to normal by active anti-diabetic treatment.

Neuralgia is often dependent upon the appearance of true neuritis. A sharp distinction between simple neuralgia and true neuritis is often very difficult to make but the following points should be borne in mind in making a differential diagnosis.

In neuritis—

(a) The pain is somewhat characteristic in that it is almost always worse at night and disturbs sleep. Burning sensation with a feeling of tingling and coldness is also common. While walking the patient gets a sensation as if he is walking on cotton wool pads. Hyperaesthesia is also often present and is sometimes so marked that the patient is unable to bear the weight of even light bed clothes.

One very noticeable symptom observed in some cases is that the patient gets much pain on light rubbing but feels relieved on deep pressure on the part.

(b) There may be paresis or even paralysis.

(c) There may be trophic disturbances such as perforating ulcer changes in the nail etc.

(d) The tendon reflexes are diminished or absent.

Treatment—It depends on individual cases.

Attention should be directed to the elimination of all septic foci as far as practicable. An active anti-diabetic treatment should be followed by a judicious adjustment of

diet and insulin, avoiding undernutrition of the patient by a too rigid restriction of diet

In some intractable cases of severe neuritic pain beneficial results have sometimes been obtained by the use of cobra venom either alone or preferably in combination of with a neurotropic antigen such as "Denurin" in suitable dosages. One however has to be very cautious in advocating this therapy

Vitamin B complex in suitable doses supplemented by thiamin chloride often does good and should be given a through trial

For the relief of the patient, hot fomentation (moist) may be ordered and anti neuralgic drugs prescribed. Infra red rays may be applied

Pulmonary Tuberculosis and Diabetes

This is one of the most dangerous complications in diabetes and unfortunately, a fairly common one in the neglected cases. The onset of tuberculosis in diabetes is usually insidious and the diagnosis of tuberculosis in its initial stage is particularly difficult to make and herein lies the danger

As soon as the physician suspects the onset of tuberculosis in diabetes he should use all the methods of diagnosis available to him, such as thorough and careful physical examination of the lungs, examination of the sputum blood count x rays etc. to make the diagnosis as certain as possible, because it is quite obvious that if anything could be done for the patient to lessen his sufferings and to prolong his life, it is at this early stage

The author thinks that he should mention in this connection that at least in three cases of diabetes of a moderate grade of severity with tuberculosis that came under his observation, the diabetic symptoms disappeared suddenly and there was an unexpected improvement in the patient's

tolerance for carbohydrates without rigorous anti-diabetic treatment

Treatment—Though this is still unsatisfactory it is to be admitted that the outlook has definitely changed for the better since the advent of insulin. Early use of insulin and control of the diabetic condition are the keynote of treatment. Such treatment should be directed to both the diabetic and tubercular conditions simultaneously. Instead of dieting the patient by the usual rule of 30 calories per kilo of the body weight these patients should have at least 40 calories per kilo the excess of carbohydrates over the patient's tolerance being covered by a sufficient amount of insulin.

For instance a diabetic patient with tuberculosis weighing 60 kilos should usually have a diet yielding 2400 calories and consisting of 160 gms C 80 gms P and 160 gms F. In special cases still further increases may be made.

Diet should however be both nutritious and easily digestible. It should be specially rich in vitamins.

Special attention should be directed towards the general hygienic condition and surroundings of the patient. Rest in bed is essential. Early sanatorium treatment should be advocated in suitable cases.

It should also be mentioned that when artificial pneumothorax phrenic avulsion etc. are necessary they should be done as in a normal person due regard being had to the control of the blood sugar prior to the operation.

Ocular Complications in Diabetes

Ocular complications have been found to be frequent in diabetic subjects and are often distressing problems. The following are some of the common complications in diabetes seen in the author's clinics arranged according to the frequency of their occurrence —

- 1 Retinal hæmorrhages and retinitis
- 2 Waxy exudates in the retina

- 3 Errors of accommodation
- 4 Senile cataract
- 5 Juvenile cataract
- 6 Iritis
- 7 Optic atrophy
- 8 Retrobulbar neuritis

It thus appears that retinitis and retinal hemorrhages are the commonest and one of the most serious complications in diabetes particularly in the elderly chronic patient. Deep retinal hemorrhages and waxy exudates often mark the primary stage of progressive diabetic retinopathy. If proper precautions and care are not taken in the early stages the ocular damage in most of the cases becomes increasingly deteriorating sometimes leading to total blindness.

The author's experience regarding the prognosis of pure diabetic retinitis (uncomplicated with such conditions as albuminuria, arteriosclerosis and high blood pressure) is however fairly satisfactory provided that prompt and vigorous treatment is undertaken on proper lines. A few cases are on record where further haemorrhages and exudates entirely stopped and further visual deterioration was prevented.

In a certain number of cases however where vascular degeneration was progressive the retinitis and the hemorrhages became worse although the diabetes was adequately controlled. These cases are fortunately few.

Treatment—Nearly all the complications of the eye are amenable to treatment if not allowed to proceed too far. An active anti-diabetic treatment is essential and the patient must be made sugar-free and the blood sugar brought down to normal. The same rule applies to cataract which can be operated upon successfully and the recovery is likely to be uneventful if proper precautions are taken to control diabetes before the operation is performed. In this connection the author would like to mention that bad cases of diabetes with marked hyperglycemia and glycosuria

often complain of their eye sight becoming gradually worse during the first few days of treatment when the aim is the rapid de-sugarization of the patient. This peculiar condition is probably due to alteration in the fluid balance of the tissues, owing to rapid changes in the concentration of the sugar in the blood and the body fluids. This naturally causes a difference in the osmotic tension and the lenses of the eyes being involved in this process cause these sudden refractive changes. The patient who would naturally be alarmed if such things happened should therefore be told beforehand about the possibility of a temporary loss of vision being at the same time assured that there is absolutely no danger attached to this temporary phase and that everything will become normal in a short time.

SOME CONTROVERSIAL QUESTIONS

The question of marriage in diabetes

Now and again the physician is confronted with the following question from his patient—Doctor is it advisable for me to marry? In the previous chapters it has been mentioned that men suffering from diabetes are often found to be impotent and the women to cease to menstruate. Both these however are usually functional in origin and are amenable to treatment if tackled early and persevered with long enough specially with the help of insulin. Some authorities lay stress on the fact that while advising patients on such important matters the possibility of the hereditary nature of the disease should be pointed out to them but at the same time too much pessimism should not be allowed to grow in their minds. The author's views regarding this have already been indicated in chapter III page 35 while dealing with the question of heredity in diabetes.

In diabetic women the possibility of the disease getting worse during pregnancy should be explained to them.

The question of pregnancy in diabetic women

It has already been stated that glycosuria in pregnancy is a frequent finding and is usually caused by the fact that in pregnant women there is an increased permeability of the kidneys to sugar and a lowering of the renal threshold. This should not however be confused with diabetes proper because the blood sugar in these cases usually remains at the normal level. In some pregnant women glycosuria which occurs is caused through the hyperactivity of the anterior pituitary during pregnancy* and the blood sugar is sometimes raised and sugar tolerance diminished though temporarily.

In dealing with the question of the presence of true diabetes in a pregnant woman a thorough investigation should be undertaken and a proper diagnosis made as early as possible. If the pregnant woman is found to be a diabetic the nature of the severity of the case should also be determined and the patient treated accordingly.

In treating the case of a pregnant diabetic woman the physician should remember the following important points —

(1) The pernicious vomiting in pregnancy in a diabetic woman may lead to severe acidosis and hence preventive and active treatment should be undertaken as soon as the early symptoms manifest themselves.

(2) The diet of pregnant diabetic women should contain more carbohydrates than in the non pregnant ones; otherwise there is a chance of ketosis to develop.

(3) In pregnant diabetic women there is an increased demand for carbohydrates during the latter part of pregnancy particularly in the last two months probably due to two main factors — (a) the foetus using up a large amount of glucose (about 30 to 50 grammes per day) which it removes from the maternal blood and (b) the additional

* Wall & Bosc *Journal of Obstetrics of the British Empire* Vol 79 No 2 1972

insulinogenic function of the foetal pancreas. These factors should be remembered with a view to making necessary adjustments regarding the carbohydrate intake and the dosage of insulin as otherwise severe hypoglycaemia is likely to develop suddenly.

(4) Severe insulin hypoglycaemic shock in the mother may sometimes lead to the death of the foetus and bring about abortion. This can certainly be avoided if proper precautions are taken.

(5) The intra-uterine mortality in diabetic woman is stated to be high.

(6) The babies born of diabetic mothers are usually of large size and hence care must be taken to determine the size of the baby beforehand and if necessary an early induction of labour or Caesarean section should be envisaged.

(7) The use of chloroform should be avoided during parturition.

The introduction of blood sugar tests and the discovery of insulin have brought about a much brighter outlook regarding these cases and we can now safely allow the pregnancy to continue till term unless of course it becomes contraindicated by inability to control the disease by a judicious combination of diet and insulin. It should however be kept in mind that in a diabetic pregnant woman there is often a tendency towards spontaneous abortion.

CHAPTER VII

DIABETES IN CHILDREN *

THE diabetic child is of more than usual interest to those working on this disease not only because it provides them with pure diabetic lesions unaccompanied and uncomplicated by any degenerative changes due to age but also because it gives them a better opportunity of following up the effects of treatment. The prognosis in cases of diabetes in children was always thought to be a matter of considerable seriousness in the past but it is not reasonable to take such a pessimistic view at the present day. There is no doubt that since the advent of insulin the outlook for these cases has been much brighter; a great deal may be done to improve the condition of the child which if it does not prolong his life will certainly make it more comfortable. This is possible because in a child the regenerative powers are at their highest and hence under proper care and suitable treatment there is much greater opportunity for the regeneration of the islet cells of the pancreas. The literature on the subject is replete with evidence that there is a much quicker regeneration of the islands of Langerhans in children than in adults. Boyd (1925) has reported an interesting case of diabetes in a boy who recovered but subsequently met with an accidental death. On autopsy the pancreas was found to be normal with the exception of scattered pyknotic nuclei in some of the island cells. Boyd had previously observed the presence of a very large number of island areas at the periphery of the pancreas sometimes twelve or fourteen in a low power field. Bensly in commenting on Boyd's paper, said that these small bulbous islands adjacent to a duct resembled those produced in ex-

* Reprinted from *The Indian Medical Gazette* Vol. LXVIII No. 8 August 1933 page 443

perimental animals by the regeneration of newly produced islands



FIG. 1

A Before treatment

B After 3 weeks of treatment

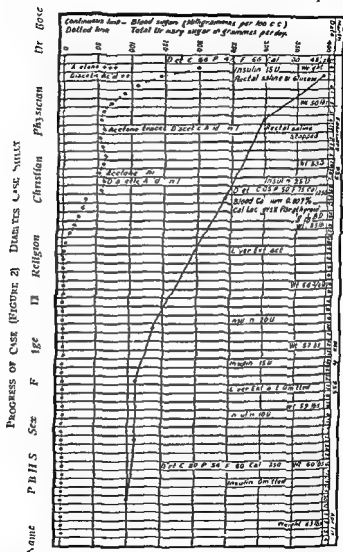


FIG. 2

A Before treatment

B After 13 weeks of treatment

It may be stated with a certain amount of definiteness that taken properly in hand, the diabetic child should make considerable improvement within a comparatively



short time. Such improvement in the general health and in the proper growth and development of the child takes

place quickly if the case is properly managed from the beginning. The improvement is sometimes so marked that the child becomes scarcely recognizable within six weeks of the commencement of the treatment. In p. 147 are photographs of two of the author's cases which lend support to this statement (figures 1, 2 and 3).

While therefore the final prognosis in cases of diabetes in children may not be predicated with any amount of certainty, one should not take too gloomy a view of the disease in the present day of insulin treatment. We know that it is possible now to turn a diabetic child from a living skeleton into a robust healthy being, but whether or not this condition can be maintained permanently, only further research can show.

Age of onset.—Diabetes in infants under one year of age is infrequent. The youngest diabetic child amongst the author's series of cases was a boy aged 1 year and 4 months. The author's experience has been that diabetes is less common in children under 5 years of age. The youngest diabetic child in Joslin's series of cases was a baby 8 months old. Ashby (1923) described the case of a four months old diabetic baby with gangrene of the toes. Major and Curran (1922) reported a case with diabetic cataract in a baby 11 months old.

Etiology.—This is still very obscure. According to many observers heredity is an important factor. Amongst most of the author's cases, however, heredity could not be traced as playing any important part in the etiology of the disease. It should be noted here that unlike diabetes in adults obesity does not seem to be of any importance as an etiological factor in diabetes in children. The author is inclined to the opinion that some inherent defect in the endocrine balance of the child leading to a disturbance in its normal mechanism is the causative factor though the exact nature of this disturbance is still obscure.

Onset.—In some of the author's cases the onset was sudden and the course was rapid. One of the cases was

diagnosed for the first time while in a pre comatose condition—the child having suddenly become ill with an eruptive fever three days previously. In other cases the onset was slow and insidious, diabetes being wholly unsuspected in the beginning. The usual history in most of these cases was that the child began to lose weight without any apparent cause and became peevish and sickly. The polyuria and unusual thirst which the child manifested was attributed to causes other than diabetes. One of these patients was treated for intestinal worms off and on for about 6 months, till he was brought to a miserable state of existence when luckily the urine was examined and found to be loaded with sugar, acetone and diacetic acid.

General considerations—The characteristics of juvenile diabetes as distinct from the adult type are mainly its severity, rapid progression and liability to sudden complications.

Diabetic children are usually found to be taller than normal children of the same age and they are usually mentally alert, sometimes verging on precocity* but at the same time, these children are undeveloped in other respects. This peculiarity has been noticed in most of the cases that came under the author's observation. They are usually sexually immature—the primary and the secondary sexual characteristics being either unusually delayed or absent altogether. In one of the author's cases a somewhat remarkable one of a girl aged 17 (see figure 1) there were no signs of catamenia, the uterus was of the infantile type, and the secondary sexual characters were

* The following note as to the special peculiarities of the diabetic children was prepared for the author by an observant staff nurse in charge of the children's ward.

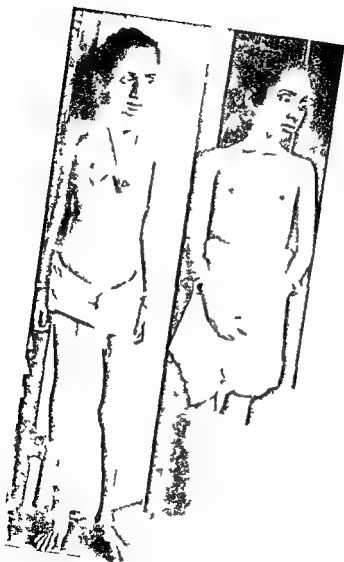
(1) Children suffering from diabetes are more intelligent than other children of the same age.

(2) They are very precocious and quick at understanding.

(3) They are inclined to be very cunning and sly in their ways.

(4) Their nature is very sensitive and great kindness and tact is required in dealing with them.

(5) At times they are depressed irritable and hysterical and need a little firm handling which usually brings them round quickly.



C a e Fc 3
Bf

absent. The girl behaved like a child of 11 or 12 only, though mentally she was very alert and more than usually intelligent and followed the line of treatment with greater understanding than those many years her senior.

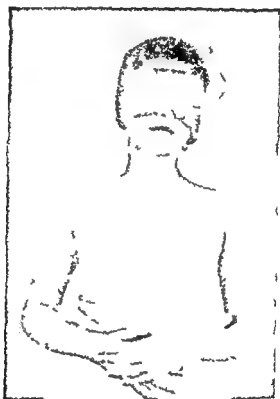


FIG. 4

Girl aged 17 years (The lack of development is apparent)

This peculiar conjunction, namely, superiority in height, precociousness and sexual immaturity, appears to the author to point to a condition which has been brought about by the absence of a proper involution of the thymus gland leading to a condition of hyperthymism.

We know that the thymus is directly antagonistic to the gonads in physiological manifestations and in the condition of hyperthymism there is almost always an associated condition of partial or total insufficiency of the gonads. We know that one of the peculiarities of hypogonadism is that if this condition takes place before puberty the skeletal development is somewhat excessive in the direction of length thus explaining the somewhat excessive length of



FIG. 5
A group of Diabetic children

lower limbs. This gives a partial explanation why the sexually immature diabetic child is usually taller than other children of the same age.

Treatment—Though the principle underlying the treatment of diabetic children is more or less the same as

that of an adult yet there is a considerable difference in many essential details. For instance it should always be borne in mind that the food requirements of growing children are proportionately much greater than those of the adult and a diet which is insufficient in its total caloric value or inadequate as regards the protein ration may cause serious harm. The growing child requires a generous diet which should not only yield the total caloric value needed according to the age of the child but should contain the proper amount of protein to maintain health and vigour and to promote growth. It should also be borne in mind that children as a rule cannot take the same proportion of fat per kilogramme of body weight as an adult and they are more liable to develop acidosis.

The essential difference between the dietetic treatment of diabetic children and adults lies in the fact that whereas in the case of adults the protein requirement under basal conditions is approximately about one gramme per kilogramme of body weight in the case of diabetic children the protein requirement varies inversely according to the age—i.e., the younger the child the greater is the protein requirement per kilogramme. The same rule holds good in the case of the carbohydrate as well as in the total caloric requirements. The fat requirement by diabetic children is also essentially different from that of an adult. The ratio of fat to carbohydrate in the diet of the former should be much less than in that of the latter because diabetic children are more liable to develop ketosis on a diet disproportionately rich in fat at the same time it should be remembered that the fat content in the diet should not be too low because fat serves as an important carrier of the fat soluble vitamin A which is essential to growth. The following table gives the approximate carbohydrate fat protein and the caloric requirements of diabetic children in the different periods of their lives. It should however be borne in mind that the proportions given below are only average and have to be varied at times according to the

nature of the case and according to complications present or arising

Age of the child	REQUIREMENTS PER KILOGRAMME OF BODY WEIGHT			
	Fat	Carbohydrate	Protein	Calories
1-2 year	3 gms	17 gr	4 gm	90
2-5	3	9	4	80
6-10	3	8	3	60
10-15	3	3	2	50

It will be seen from the above table that the caloric requirement per kilogramme of body weight as well as the protein and the carbohydrate requirements increase inversely according to the age—the younger the child the greater is the food and the caloric requirement per kilogramme of the body weight. The fat requirement however has been kept at an arbitrary figure of 3 grammes per kilogramme but the ratio between the fat and carbohydrate in the diet has been altered by proportionately increasing the carbohydrate quota of the diet. For instance it will be seen that the proportion of fat to carbohydrate in the first two years of life has been kept as low as 1 to 4. As the age increases the proportion of fat has also been increased in relation to the carbohydrates so that at the end of the table a child between the ages of 10 to 15 years gets a proportion of 1 to 1 which approaches the normal adult proportion.

It should also be remembered by the doctor prescribing diets for diabetic children that he must take into consideration the suitability of the food stuffs according to the age of the child. For instance the diets of infants under 2 years should mainly consist of milk. For bigger children eggs fish potatoes bread butter vegetables fruits etc. should be prescribed.

Insulin therapy—The principle of the treatment is the same in children as in adults. If the case is an uncomplicated one and of mild nature and if the blood sugar is not excessively high, the effect of dieting alone should be tried for a few days, in order to see whether this alone has an effect in reducing the blood and urinary sugar, and in improving the general health of the child. If dietetic treatment, continued for about a week, fails to make any impression or if the child loses weight, insulin should be commenced. Of course, if the case is of a severe nature, or if there are complications insulin treatment should be started at once.

Regarding the dosage of insulin, no hard and fast rule can be laid down but in as much as the dose may vary in individual cases it should be mentioned here that in children, the *proportionate* dose of insulin per kilogramme of body weight is usually higher than in adults because of the high carbohydrate content of their diet. It should also be remembered that some of the diabetic children require relatively big doses to make their urine sugar free. One of the author's cases, a child aged 5 years and weighing only 33½ pounds (or approximately 15 kilogrammes) required as much as 30 units of insulin daily (given in two doses) to make his urine sugar free.

As a general routine, however, it can be laid down that in mild cases uncontrolled by diet alone, it is best to commence with small doses of, say, 2 to 3 units once or twice daily. In more severe cases, with high blood sugar, commence with 5 to 6 units twice daily. As in the case of adults the dose should be increased gradually until the glycosuria disappears and the blood sugar becomes normal.

It must be remembered that in treating cases of diabetes in children, not only must the urine be kept sugar free and the blood sugar kept within normal limits but very careful attention must be given to the proper growth and development of the child. The child must grow in height and gain in weight like other normal children. In

cases where the urine is made sugar free but the child does not grow or gain in weight the diet must be raised and extra doses of insulin given to keep the urine sugar free on the other hand if the gain in weight is abnormally rapid the diet should be cut down and the dose of insulin adjusted accordingly

Prognosis—It is undoubted that insulin has made a great difference in the prognosis. It has not only helped to make their lives comfortable but it has prolonged the lives of these children and made it possible for them to grow and develop almost normally. Joslin's statement with regard to this point is very apposite he says Thirty years ago when I began treating diabetic children I counted the days they lived. It is hard to believe but it is true that I am now beginning to measure their lives in decades.

CHAPTER XIII

GLYCOSURIA AND LIFE INSURANCE

It frequently happens that a person otherwise hale and hearty is refused insurance on his life by some of the reputable insurance companies because the medical report indicates the presence of a reducing substance in the urine. The matter is no doubt very important from the point of view of the company which has every right to safeguard its own interests but it is also of vital importance to the prospective insured person whose only chance of making some provision for his family in the event of his sudden death happens to be an insurance on his own life.

There are two essential points to which the attention of the medical officers of insurance companies should be drawn and on which they must satisfy themselves before they can do full justice to the company and its client either by accepting or refusing the life of the proposer.

He will have to find out —

(1) Whether the reduction of the copper salts is due to sugar or some other reducing substance which may be present in the urine. It should be borne in mind that the substances which reduce the copper solution may be many, the common amongst them being some of the drugs including rhubarb, senna, amidopyrine, ascorbic acid etc. high concentrations of the normal urinary constituents including creatinine, uric acid etc. glycuronates or some of the abnormal metabolic urinary constituents such as homogentisic acid.

(2) In case	that a	substance is
sugar the next	le is	s glucose or

detect on

any other form of sugar such as laevulose lactose galactose pentose etc

If however it is found that glucose is present in the urine the next point to decide is whether the patient is a true diabetic or the glycosuria is non diabetic in origin mention about which has already been made in the text previously

In usual practice however most insurance companies depend on the urinary sugar as the criterion for the diagnosis of diabetes and usually reject cases which show glycosuria on routine examination

This procedure could have been excused in the old days when the diagnosis of diabetes mellitus mainly depended on the presence of sugar in the urine and thus the proposals of many innocent non diabetic individuals were either declined or accepted under special circumstances as to short term and high rates

But this crude method of diagnosing diabetes by the mere presence of sugar in urine has no excuse in these days when we have so many modern means at our disposal for the purpose of finding out not only whether the person under investigation is a true case of diabetes mellitus but also in case it proves to be diabetes at what stage it is Every medical officer of an insurance company should make it his business to investigate the doubtful cases because if that is not done it may mean considerable injustice to particular individuals and an innocent non diabetic person may be classed as a diabetic The medical officer who through over caution (in the interest of the company) or indifference rejects a proposer on the basis of the copper test alone prejudices him in the eyes of other insurance companies whom he may approach subsequently and thus he is either rejected again or unjustly overloaded On the other hand if by proper and thorough investigations it is found that there are signs of the beginning of diabetes in a young proposer the medical officer has every right and

it is his duty to reject the person in question, because the company has to view the proposer not as he is at present but as he is going to be. It has absolutely no power to control the conditions under which the proposer may live nor assume that by suitable anti-diabetic treatment, he may ward off the disease.

In cases of diabetic glycosuria in the aged the outlook is somewhat different. Here, if proper discretion is used by the medical officer, he may, after a thorough investigation into the history and the progress of the disease, recommend the proposal for acceptance, subject to special conditions as to premium, etc., or reject it altogether.

There is another important matter which an insurance doctor would do well to remember, namely, that it is often a matter of chance whether sugar is detected in the urine or not. If the proposer is a mild case of diabetes and appears for examination in a fasting condition no sugar will probably be found in the urine. If he comes 2 to 3 hours after a full meal he will probably pass a fair amount of sugar in the urine. It is mainly for this reason that the patient gets puzzled by being told by one doctor that there is sugar in his urine, while another equally competent medical man tells him that there is none. The relation of glycosuria and hyperglycæmia to the meals taken has been described in Chapter VII.

To safeguard the interest of the company and to be equally just to the proposer, the medical officer in doubtful cases should—

- (1) make the person drink 50 to 100 grammes of glucose dissolved in about 4 oz. of water in his presence, and after about 2 hours collect a specimen of his urine and examine for sugar,
- (2) test the fasting level of blood sugar of the patient or, better still, do a glucose tolerance test.

Attempts at fraud practised by proposers on insurance companies—Attempts are now and then made by diabetic individuals to pass the tests of the insurance doctor by fasting themselves for periods varying from 18 hours onwards to make themselves sugar free at the time of the examination. If there is suspicion to this effect the examiner should test the urine for acetone bodies which if present would confirm the suspicion. A test meal of glucose should be given to the patient in these circumstances and the urine examined about 2 hours after. If possible a glucose tolerance test should be done.

In these modern days of insulin a diabetic individual may seek the help of a doctor and fortify himself by suitable adjustment of diet and insulin before appearing for examination by the insurance doctor. Here too the glucose tolerance test will clear the diagnosis in cases of doubt.

If every candidate for life insurance appearing for medical examination be made to take about 3 ounces of glucose dissolved in water and the urine collected and tested for sugar about 2 hours after much trouble worry and unpleasantness would in the opinion of the author be saved. A solution of glucose of suitable strength may be kept in stock. As soon as the patient appears before the doctor he may be asked to empty his bladder and immediately afterwards receive the drink of glucose. The medical man meanwhile may go on with the other examinations. At the end of 2 hours he collects another specimen of urine and tests both samples. If this is carried on as part of the routine work the patient never suspects anything but thinks that the drink that is offered to him is part and parcel of the usual test. On the other hand the doctor receives much valuable information which would not otherwise be available to him. In cases where even this procedure leaves room for doubt the patient may be made to undergo a more crucial test.

CHAPTER XIV

A SIMPLIFIED METHOD FOR ESTIMATION OF SUGAR IN BLOOD *

THAT normal blood contains sugar was known even before the time of Claude Bernard and since then numerous methods have been devised by workers all over the world to estimate the sugar many of these being obsolete by now. Formerly, the estimation of sugar in the blood used to be a tedious process but now a days it is comparatively simple. Even then however nearly all the methods for blood sugar estimation require a well fitted laboratory and a fairly well trained worker to carry out the test.

The importance of blood sugar as a factor for consideration has increased enormously since the insulin treatment has come into use. All cases of diabetes undergoing insulin treatment require periodical sometimes daily examination of blood sugar. In large cities like Calcutta with well equipped hospitals and laboratories and trained workers in them, this is always possible, but the same cannot be said of the distant mofussil towns and villages in some of which even a qualified medical man is wanting.

A doctor in such a place is very much handicapped in treating a case of diabetes with insulin not being able to get any idea of what the initial blood sugar level is and also what changes take place in the blood sugar during insulin treatment. It has been suggested that where blood sugar estimation is not possible, insulin treatment can be carried out by relying on the urinary sugar only. This appears to us to be an unscientific and sometimes a dangerous procedure. Reference has already been made to a few cases of renal glycosuria treated with insulin with results

* Demonstrated by the author at the Scientific Exhibition of the Seventh Congress of the Far Eastern Association of Tropical Medicine December 1927

just short of disaster. Even in a case of diabetes one does not get a clear indication about the proper dose of insulin to be injected and also about the interval of time between injections without a knowledge of the patient's blood sugar and this is essential for successful treatment of diabetes mellitus. To give too small a dose of insulin and at too long intervals will not do much good to the patient; to give an overdose of insulin on the other hand may mean trouble.

In order to help medical practitioners in mofussil towns and villages to carry out insulin treatment successfully by regular blood sugar tests the author has devised* a simplified method for the estimation of the sugar content of blood which would be fairly accurate for clinical purposes and at the same time sufficiently easy and quick for the average busy practitioner to carry out. Controls by authenticated blood sugar methods show that the results obtained are quite accurate for clinical purposes.

General principle of the method

- (1) Precipitation of the protein and the colouring matter of the blood by means of precipitating reagents and then filtering it
- (2) Boiling the crystal-clear blood filtrate (containing glucose) with alkaline copper solution so as to get the copper reduced by the sugar in the blood
- (3) Getting a blue coloured compound† by the interaction of phospho-molybdic acid and the reduced copper

* The complete apparatus is manufactured by the Bengal Chemical & Pharmaceutical Works Ltd. Calcutta.

† When not

the intensity of the blue colour developed being directly proportional to the amount of reduced copper present which again is dependent on the amount of sugar present.

- (4) Comparison of the blue colour thus produced with the colour produced by a standard glucose solution of known strength, similarly treated. This is done by means of a comparator devised for the purpose. Dilution has to be made of the deeper coloured solution until both the solutions match exactly in colour, the amount of dilution made is then noted and the result read off from the table.

Apparatus required

- (1) Test tube rack
- (2) Ordinary glass tube for making oxalated tubes *
- (3) Test tubes (size 4 inches by $\frac{1}{2}$ inch) for collecting oxalated blood
- (4) Pipette (3 c.c.) with three divisions for measuring distilled water
- (5) Extraction tubes (2 inches by $\frac{3}{4}$ inch) for extracting blood in distilled water and for filtering the same after precipitation
- (6) Pipette (0.2 c.c.) with one mark for measuring blood for estimation of sugar
- (7) Pipettes (0.4 c.c.) with one mark for measuring the two precipitating reagents
- (8) Small glass rods for stirring up the blood after precipitation
- (9) Small funnel, filter papers (starch free—5.5 cm.) for filtration of blood after precipitation
- (10) Measuring flask (50 c.c.) for making up "stock" and "standard" glucose solutions
- (11) Pipettes (1 c.c.) with one mark for preparing and measuring "standard" glucose solution
- (12) Graduated tubes (30 c.c.) for boiling the "standard" glucose and the "blood filtrate" with copper solution
- (13) Pipettes (2 c.c.) with one mark for measuring out blood filtrate, alkaline copper solution and phosphomolybdic acid solution
- (14) Tripod stand, copper water bath and spirit lamp for boiling purposes
- (15) Comparator (Fig. 5)

* The easiest way of preparing an oxalated tube is to blow into the test tube with a glass tube and then to sprinkle some finely powdered neutral potassium oxalate inside. The inner walls of the tube thus becoming moist through a uniform layer. Care should be taken that the potassium oxalate precipitant being roughly.

In cases where the sodium fluoride should

Reagents required

- (1) Powdered potassium oxalate (neutral), for preparing oxalated tubes
- (2) Sodium tungstate (pure crystals) 10 per cent solution
- (3) Acid sulphuric—2½rd normal solution
- (4) Alkaline copper solution, which is prepared as follows —
Dissolve 40 grammes of pure anhydrous sodium carbonate in about 400 c.c. of distilled water with the aid of heat if necessary. Dissolve 45 grammes of "extra pure" copper sulphate crystals in about 100 c.c. of distilled water. Mix the two solutions thoroughly in a litre flask. Dissolve 75 grammes of pure tartaric acid separately and add the solution to the flask. The receptacle in which the copper sulphate is dissolved must be repeatedly washed in distilled water and the washings added to the flask. When cool distilled water should be added and the solution made up to the mark. Filter
- (5) Phospho-molybdic acid solution, prepared as follows —
Dissolve 35 grammes pure molybdic acid (free from ammonia) in 200 c.c. of 10 per cent sodium hydroxide solution. Add another 200 c.c. of distilled water and boil until all traces of ammonia are driven off. (This can be tested by presenting a glass rod dipped in strong hydrochloric acid.) Cool and add 125 c.c. of phosphoric acid (85 per cent). When sufficiently cool make up to 500 c.c. with distilled water
- (NB—This solution should be of such a strength that 2 c.c. of this will completely discharge the blue colour from 2 c.c. of the alkaline copper solution. It is advisable to test these reagents occasionally and to make blank experiments with them from time to time.)
- (6) "Stock" glucose solution—1 per cent, prepared as follows —
Take two Grape Sugar Tablets (Merck), each containing 0.25 gramme of glucose directly into the 50 c.c. measuring flask. Fill half the flask with a saturated solution of benzoic acid. Shake the flask till the tablets dissolve completely and then fill the flask up to the mark with saturated benzoic acid solution. The solution should be bottled and kept well stoppered. This solution will keep proper strength for about a month
- (NB—To prepare "standard" glucose solution from the stock, wash out the 50 c.c. flask with distilled water thoroughly. Measure out 1 c.c. of the "stock" glucose solution by means of the 1 c.c. pipette and deliver it into the flask. Make up to the mark with distilled water and shake well. This solution should be made fresh each time. 1 c.c. of this solution will contain 0.2 milligramme of glucose.)

Method of estimation

With the usual aseptic precautions draw $\frac{1}{2}$ to 1 cc of blood from the vein. With a little practice this small amount of blood can also be collected from a deep prick of finger or the ear lobe (capillary blood). To obtain this the patient should be instructed to dip the hand in warm water and after thorough drying to swing the arm vigorously backwards and forwards for a little while. Rub the finger tip thoroughly with cotton wool soaked in ether and make a fairly deep puncture with a sterilized sharp surgical needle. (An ordinary sharp intravenous needle serves the purpose as well.) If the puncture is done quickly enough very little pain is felt. A good flow of blood can be obtained by squeezing the finger in a proper and systematic way. The blood may be collected either directly in the 0.2 cc pipette (by capillary action) or into the ovalated tube from which the blood can be measured out.

In an extraction tube measure out 3 cc of distilled water by means of the 3 cc pipette. Accurately measure out 0.2 cc of blood by means of 0.2 cc pipette and deliver it into the extraction tube. Shake lightly and wait till all corpuscles become laked and the solution becomes clear red (Plate I A).

Now add 0.4 cc of 10 per cent sodium tungstate solution followed immediately by 0.4 cc of 2/3 N sulphuric acid by means of the two 0.4 cc pipettes and stir with a glass rod. The addition of sodium tungstate and sulphuric acid precipitates the protein and the colouring matter of the blood. The precipitate is reddish at first but soon becomes viscous and turns greyish brown (Plate I B).

When the precipitation is complete the solution is filtered through the starch free filter paper. The filtrate obtained should be crystal clear. For the estimation measure out 2 cc of the clear filtrate into the special graduated 30 cc tube marked blood filtrate by means of 2 cc pipette. Into the other 30 cc graduated tube marked

standard glucose', take 1 c.c. of the standard glucose solution by means of another 1 c.c. pipette with one mark and add 1 c.c. of distilled water to it. Now add 2 c.c. of alkaline copper solution to each of these two tubes by means of a 2 c.c. pipette. Shake the two tubes by gently stroking the bottom of the tubes against the palm of the hand.

The two tubes are now introduced into the copper water bath in which water is already boiling and allowed to remain there for 10 minutes. They are then removed from the bath and the contents will be found to be of bluish colour with a reddish brown precipitate of cuprous oxide at the bottom of the tube. Two c.c. of phospho-molybdic acid solution is then immediately added to each of the two tubes

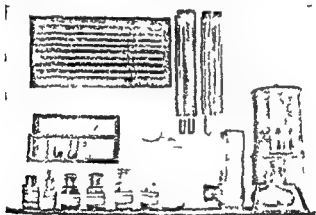


FIG. 5

Blood-sugar apparatus devised by the author

by means of a 2 c.c. pipette. A brisk effervescence occurs and the solutions in the two tubes turn deep blue. Phospho-molybdic acid as has already been stated discharges the blue colour of unreduced copper but will deepen the colour by combining with the reduced copper oxide. The intensity of the blue colour developed is directly proportional to the amount of the reduced copper

present which again is dependent on the amount of the sugar present. Shake the two tubes by slightly inclining the tubes and tapping the bottom against the palm of the hand. The solution in each of the two tubes should stand at the 11 c.c. level.

Now put these two tubes inside the Comparator (Fig. 5) and add distilled water very carefully to the tube having a deeper colour (either the standard or the blood filtrate in whichever tube the colour of the solution is deeper). Dilution with distilled water is carried on until the two solutions are matched in colour exactly. After addition of distilled water each time mix the contents thoroughly by putting in the cork and inverting the tube.

Calculations

It has already been mentioned that the intensity of the blue colour after addition of phospho molybdic acid depends on the amount of the reduced copper present which in its turn is in proportion to the amount of sugar present in the contents of the two tubes.

Now when the solutions in the two tubes are exactly matched in colour it may be assumed that the *concentration* of sugar in both of them is the same but the *quantity* of sugar present in each will vary in direct proportion to the respective volumes of the solutions. In the present case the solution in the tube marked S is known to contain 0.2 mgm. of sugar and from this the concentration of sugar in the other is easily found out by calculation.

Let us take a concrete example. Let us suppose that the solution in the standard tube is deeper in colour and had to be diluted up to 12 c.c. to match exactly in colour with the 6 c.c. of the solution in the blood filtrate tube. Here although the concentration of sugar in two solutions is the same the quantity of sugar present in the standard tube is double of what is present in the unknown tube the quantity being directly proportional to the volumes of the solutions contained in the two tubes.

We know that the 12 cc of the solution in the standard tube contains 0.2 mgm of glucose. Therefore the sugar content of the 11 cc of the solution in the unknown is half i.e., 0.1 mgm.

The proportional contents of the sugar in the unknown solution is thus readily calculated by simple rule of three —

Standard	Unknown	Strength of glucose	
12 cc	6 cc	0.2 mgm	x
$x = \frac{6 \times 0.2 \text{ mgm}}{12}$		= 0.100 mgm	

It will be remembered that originally 0.2 cc of blood was taken for experiment and was made up to a total volume of 4 cc, after filtration only 2 cc were taken for estimation. Therefore the quantity of blood actually taken for experiment was 0.1 cc.

Now if 0.1 cc of blood contains 0.1 mgm of sugar 100 cc of blood will contain 100 mgm which is equivalent to 0.1 gm (per cent).

Suppose however that the solution in the blood filtrate tube is deeper in colour and has to be diluted to 8 cc to match in colour with the solution in the standard tube. As the quantity of sugar in the two solutions will be proportional to their respective volumes and as the 6 cc of the standard solution contains 0.2 mgm of glucose the amount contained in the 8 cc of the unknown solution can be found out as follows—

Standard	Unknown	Strength of glucose	
6 cc	8 cc	0.2 mgm	x
$x = \frac{8 \times 0.2 \text{ mgm}}{6}$		0.266 mgm	

Now 0.1 cc of blood contains 0.266 mgm of glucose. Therefore 100 cc of blood will contain 266 mgm which is equivalent to 0.266 gm (per cent).

For easy calculation the author has worked out a table which will give the results at a glance. Simply note the

readings of the standard and that of the unknown in ccs and find out from the table the percentage of blood sugar at once without going into calculations

For the sake of convenience the estimation of blood sugar may be summarized, as follows step by step —

(1) Take 30 c c of distilled water in an extraction tube

(2) Measure out 0.2 c c of the oxalated blood and add it to the distilled water. Mix thoroughly

(3) Add 0.4 c c of 10 per cent sodium tungstate, immediately followed by 0.4 c c of 2/3N sulphuric acid in the extraction tube containing blood. Stir with a glass rod

(4) Filter into another extraction tube (*During the time when the filtration is going on, the "standard" glucose solution may be prepared*)

(5) Into the special 30 c c graduated tube (marked "standard glucose") take 1 c c of the standard glucose solution (containing 0.2 mgm of glucose) and add 1 c c of distilled water to it. Into another similar tube, (marked 'blood filtrate') take 2 c c of the blood filtrate

(6) Add 2 c c of the alkaline copper solution to each of these tubes. Shake

(7) Put both these tubes in the *boiling* water bath* for 10 minutes

(8) Take the two tubes out of the water bath and add 2 c c of Phospho molybdic acid to each. The solutions in the two tubes turn blue. Shake by gently stroking the bottom of the tubes against the palm of the hand

(9) Put the two tubes inside the 'Comparator', and add distilled water very carefully to the deeper coloured solution till the colours in the two tubes exactly match each other

(10) Take the readings in the two tubes in c c, and calculate or read the results directly from the table

* To save time it is advisable to set the water bath boiling just before starting the experiment

TABLE I
Solution in "Standard" tube diluted

Reading in 'standard' tube in c cs	Reading in 'blood filtrate' tube in c cs	Result (Percent age)	Reading in standard tube in c cs	Reading in blood filtrate' tube in c cs	Result (Percent age)
60	60	0.200	11.1	60	0.108
61		0.196	11.2		0.107
62		0.193	11.3		0.106
63		0.191	11.4		0.105
64		0.197	11.5		0.104
65		0.184	11.6		0.103
66		0.182	11.7		0.102
67		0.179	11.8		0.101
68		0.176	11.9		0.100
69		0.174	12.1		0.099
70		0.171	12.2		0.098
71		0.169	12.3		0.097
72		0.167	12.4		0.097
73		0.164	12.5		0.096
74		0.162	12.6		0.095
75		0.160	12.7		0.094
76		0.158	12.9		0.093
77		0.156	13.0		0.092
78		0.154	13.2		0.091
79		0.152	13.3		0.090
80		0.150	13.4		0.089
81		0.148	13.6		0.088
82		0.146	13.8		0.087
83		0.141	13.9		0.086
84		0.143	14.1		0.085
85		0.141	14.2		0.084
86		0.139	14.4		0.083
87		0.138	14.6		0.082
88		0.136	14.8		0.081
89		0.135	15.0		0.080
90		0.133	15.2		0.079
91		0.132	15.4		0.078
92		0.130	15.6		0.077
93		0.129	15.8		0.076
94		0.127	16.0		0.075
95		0.126	16.2		0.074
96		0.125	16.4		0.073
97		0.123	16.6		0.072
98		0.122	16.9		0.071
99		0.121	17.1		0.070
100		0.120	17.4		0.069
101		0.119	17.7		0.068
102		0.118	18.0		0.067
103		0.116	18.2		0.066
104		0.115	18.5		0.065
105		0.114	18.8		0.064
106		0.113	19.1		0.063
107		0.112	19.4		0.062
108		0.111	19.7		0.061
109		0.110	20.0		0.060
110		0.109			

With the usual aseptic precautions draw 1 to 2 c c of blood from the vein and collect the blood directly into an oxalated tube. Mix well and if the examination is not likely to be done within a few hours add 1 drop of 10 per cent formalin as a preservative.

Another method of preserving blood samples is to mix 3 parts of powdered potassium oxalate with 1 part of potassium fluoride. Take 0.01 gm of this mixture in a clean test tube and collect 1 c c of blood directly into it. Mix thoroughly and send out to the laboratory for examination.

CHAPTER XV

EXAMINATION OF THE URINE

ALMOST invariably, the first diagnosis of glycosuria or diabetes is made from the examination of the urine. Diabetes is a very insidious disease and, when sugar appears in the urine, it may be taken for granted that the disease has made some progress in the system. It has to be borne in mind that the detailed tests for the proper diagnosis of diabetes in the prediabetic stage are not always possible owing to a variety of causes but a systematic examination of the urine can always be made by every doctor at the bedside or in the laboratory. If it is done carefully and systematically many cases of true diabetes would be detected at a comparatively early stage when the disease is more amenable to treatment.

Everyone will admit that when diabetes has advanced so far as to present the usual symptoms and when the patient passes sugar albumin or acetone in the urine the disease is in a fairly advanced stage and the chances of recovery are remote. If every practitioner—medical surgical or gynaecological—would make it a rule to have the urine of their patients examined for sugar, albumin and acetone at the earliest opportunity, many cases of diabetes would be averted and many patients would be spared the serious complications which are so often foreseen.

It is in the morning that the urine should be examined. This may lead to the discovery of sugar in the urine of men (who have dinner) or of women (who get either a meal or a

It should be remembered however that examination of single specimens of urine and the determination of the "percentage" of sugar present therein is often fallacious because it will naturally vary according to the previous diet of the patient and the dose of insulin if administered. It certainly does not give any idea as to the total sugar loss of the patient in 24 hours. The most important thing is to find out how many grammes of sugar the patient is excreting in 24 hours. The method followed by the author has been described in Chapters IX and X.

For the purpose of following up a case the method of calculating the total sugar excretion in grammes in 24 hours will be found very helpful in the proper adjustment of the diet and the dosages of insulin in individual cases.

Sugar in normal urine

It has been proved beyond doubt that normal urine contains some amount of glucose. The amount present is so small that it is not sufficient to give a positive result with Fehling's or Benedict's test. Folin Myers, Benedict Osterberg and a few others worked on this subject and they succeeded in finding various methods for detection and estimation of sugar in normal urine. The author also worked on this line in collaboration with the late Dr Mackenzie Wallis at St Bartholomew's Hospital in London and they were able to find a new and reliable colorimetric method for the estimation of sugar in normal urine*. As a result of analysis of about 200 samples of normal urine in Europeans by this new method they found that the concentration of sugar in urine varied between 0.06 and 0.09 per cent amounting to a total of 0.8 to 1 gramme in twenty four hours. In normal healthy Indians the range of variation according to the author's findings is from 0.06 to 0.10 per cent.

* Glucosuria in pregnancy. *Journal of Obstetrics and Gynaecology of the British Empire*, Vol. XXIX, No. 2 Summer 1922 (Wallis and Rose).

Benedict's qualitative test for sugar

This is a comparatively simple test for sugar in urine and it has at present displaced nearly all other reduction tests for sugar. It is a single solution and keeps for a fairly long time.

One of its chief advantages over other methods is that it tells us at once the approximate percentage of sugar in the urine from the character of the precipitate formed. It is of great value, therefore to the busy practitioner, for it readily gives him a rough idea of the amount of sugar the patient is passing.

Preparation of Benedict's solution—Weigh out 173 grammes of pure sodium citrate and 100 grammes of pure anhydrous sodium carbonate and dissolve them together with the aid of heat in about 700 c.c. of water. Filter this solution. Weigh out 17.3 grammes of pure crystallized copper sulphate and dissolve separately in about 100 c.c. of distilled water. Mix the two solutions with constant stirring and when cold make it up to 1 litre.

Things required for sugar test —

- (i) Test tubes (hard glass)
- (ii) Medicine dropper
- (iii) Five c.c. measuring cylinder
- (iv) Benedict's qualitative reagent
- (v) Spirit lamp

Measure out 5 c.c.* of Benedict's solution by means of the measuring cylinder and pour it into a test tube. By means of the medicine dropper, take out the urine and put 8 drops into the test tube and boil it over the spirit lamp for about one minute or immerse the tube in boiling water for about 3 minutes.

If the solution remains clear, it should be assumed that there is no excess of sugar.

But if there is a precipitate, it is evidence of reduction of the copper by the sugar the quantity of which depends on the colour of the precipitate. Thus —

A pea green opacity represents about 0.2 per cent of sugar.

A distinct greenish precipitate means 0.5 per cent.

A distinct greenish brown precipitate means 0.5 per cent to 1 per cent.

A yellow precipitate means 1.0 per cent to 1.5 per cent.

A red precipitate means 2.0 per cent or over.

Above this percentage the colour of the solution gives little aid.

* In the absence of the measuring cylinder, a teaspoonful and a half of Benedict's solution will do.

*Mode of estimation of sugar by Benedict's original method**Preparation of the solution —*

Weigh out 200 grammes of pure potassium citrate and 100 grammes of anhydrous sodium carbonate and dissolve them together with the aid of heat in about 600 c.c. of distilled water. Dissolve 125 grammes of pure potassium sulphocyanide separately in about 150 c.c. of distilled water. Mix thoroughly and filter if necessary. Weigh out 18 grammes of pure crystallized copper sulphate and dissolve separately in 100 c.c. of distilled water and pour this into the other solution slowly small quantities at a time with constant stirring. Add 5 c.c. of 5 per cent potassium ferrocyanide and then distilled water to make the total volume 1000 c.c.

Method of analysis

If the qualitative test indicates a low percentage of sugar the urine may be used undiluted otherwise 10 c.c. of the urine should be diluted to 100 c.c. and this solution used for titration.

The urine diluted or undiluted is poured into a 25 c.c. or 50 c.c. burette up to the zero mark. Twenty five c.c. of the Benedict's quantitative reagent are measured by a pipette into 250 c.c. beaker or flask in which 3 to 4 grammes of anhydrous sodium carbonate is then added. A few glass beads or pumice stone may be kept in the flask to prevent frothing and bumping. The Benedict's solution with the added sodium carbonate in it is then heated over a flame till all the carbonate is in solution. The urine is now run in from the burette till a bulky chalky white precipitate forms and the blue colour of the Benedict's solution lessens perceptibly in intensity. From this point the solution from the burette must be run in *very slowly* a few drops at a time until the last trace of the blue colour entirely disappears. It should be noted that the solution must be kept constantly boiling throughout the entire titration.

Calculation

Twenty five c.c. of Benedict's solution is reduced by exactly 0.05 gramme of glucose, therefore, the percentage of sugar in the undiluted urine would be $\frac{0.05}{x} \times 100$ where x denotes the number in c.c. of the undiluted urine required to effect the titration. In the case where diluted urine is used the result has to be multiplied by 10.

Albumin in urine

The urine should be filtered quite clear and must be acid in reaction.

Nitric acid test—Pour nitric acid into a test tube to a depth of $\frac{1}{2}$ inch incline the tube nearly horizontal and slowly run about double

the quantity of urine down the side of the tube. Gently bring the tube to vertical position. A white deposit immediately above the acid in the shape of a clear ring indicates albumin.

N.B.—Compound proteins (albumoses or nucleo-albumin or mucin) also gives a ring, but it appears a short distance above the nitric acid layer and is rather diffused. If there is any doubt, it is best to have it verified by special confirmatory tests.

Salicyl sulphonic acid test—If the urine is alkaline make it faintly acid by adding 10 per cent solution of acetic acid drop by drop. If the urine is cloudy, filter it.

Take 5 c.c. of urine each in two narrow test tubes. Add 4 or 5 drops of a 20 per cent solution of salicyl sulphonic acid in one of them. If small amounts of albumin are present an opalescent cloudiness appears, which can be compared with the untreated urine in the control tube. If large amounts are present a pronounced turbidity or a heavy precipitate forms.

Saccharine test*—The reagent used for the test is a saturated solution of saccharine in water and is performed in the same way as the Heller's test, over which it possesses certain advantages in that it does not precipitate mæcin, urea and urates.

Ketones (acetone bodies) in urine.

Rothera's test—Take about 2 inches of urine in a test tube and saturate it with crystals of ammonium sulphate. Add about 5 or 6 drops of freshly prepared 10 per cent solution of sodium nitro-prusside. Shake gently. Carefully add liquor ammonia fortis on the top of this solution. If acetone is present, a violet colour appears which slowly or quickly changes to a deep permanganate colour according as the amount of acetone present is small or large. This test gives a reaction with diacetic acid as well.

Gerhardt's test for diacetic acid—To about 1 inch of urine in a test tube add a few drops of 10 per cent solution of ferric chloride. A precipitate of ferric phosphate occurs first but on addition of a few drops more of ferric chloride, the precipitate dissolves. If it does not dissolve filter the urine. The development of a port wine colour indicates the presence of diacetic acid.

This test is not given by acetone but it should be remembered that salicylates and carbolic acid might give a positive test but the red colour does not disappear by boiling.

* This simple test was first discovered and described by the late Dr. Chunilal Bose, C.B., I.S.O., in *The Indian Medical Gazette* (Vol. L^{IV}, p. 17, Jan. 1929) and gave fairly reliable results and is recommended as a valuable bed-side method.

Other reducing substances in the urine—identification of glucose by fermentation and other tests

When glucose is present in the urine in abnormal amounts, its detection by any of the well known methods is a simple matter. It is only when sugar is present in small quantities, so as to give a 'doubtful reaction' by the reduction tests that great difficulty is sometimes experienced in determining whether the reduction in the copper is due to the presence of sugar or to other reducing substances sometimes present in the urine. We know that the substances present in the urine which may reduce copper salt (and often mistaken for sugar) are many and among others the following may be mentioned —

(1) Some of the normal constituents of the urine such as uric acid, creatinine, etc., which, when present in excess, reduce copper solutions like sugar.

(2) Conjugated glycuronates which are hydrolyzed to reducing substances by the alkalis, especially NaOH present in the copper reagents for sugar.

(3) Carbohydrates other than glucose such as lactose, levulose, maltose, pentose, etc.

(4) Certain drugs eliminated by the kidneys such as chloral, chloroform, morphine, copaiba, salicylates, benzoic acid, sulphonal, salol, turpentine, etc.

(5) Homogentisic acid* present in alkaptonuric urine.

The determination of the question whether the reducing substance present in the urine is glucose or any of the other substances just described is often a difficult matter. There are many reagents for detection of sugar such as Fehling's, Benedict's, Nylander's etc. The author has described the merits and demerits of these reagents in one of his papers published about 22 years ago†. Without going

* Bose, J. P., and Ghose, S., *Indian Med Gaz* 1929 Vol LXIV, p. 61.

† Reducing substances in the urine. Their detection and identification, *The Indian Medical Gazette*, Vol LXI, April, 1926.

into details it would be sufficient to say that Benedict's test has been found to be of more value than any of the other reduction tests for sugar. This test however, does not differentiate between glucose and other forms of sugar.

If there is doubt as to whether the reducing substance is sugar or not the simplest course is to proceed as follows —

(1) First a preliminary Benedict's test is done to see if there is any reduction of copper, indicated by the formation of a definite *precipitate* of cuprous oxide (Cu_2O)

(2) In the case of a doubtful reduction proceed by way of fermentation by Brewer's yeast. Either a small Einhorn fermentation tube or even a ureometer will do for the purpose.

To perform the fermentation test roughly in the consultation room add a small quantity of acid tartaric to the urine (to prevent putrefaction). Take the specific gravity of the urine and add some baker's yeast to it and leave it in a warm place for 24 hours. Take the specific gravity of the urine again next day and if there is no appreciable reduction in the specific gravity, it may be assumed that glucose is not present.

(3) Follow up by special confirmatory tests if necessary.

The fermentation test is a very reliable test. If it yields negative results that is if there is no evolution of CO_2 and no reduction of the specific gravity, it conclusively proves that the reducing substance present is not glucose but may be any of the other varieties including the drugs described above. It may also be lactose, pentose or glycuronic acid.

If, however, the test is positive it indicates the presence of sugar—either glucose, levulose or maltose. In that case the strong presumption is that glucose is present in the urine, because the other two sugars fermentable by yeast rarely occur in the urine by themselves and if present they are usually accompanied by glucose as well. To make it doubly sure an osazone test for maltose and a special test for levulose may be done separately.

APPENDIX.

A

HYGIENE FOR DIABETIC PATIENTS

Physical exercise—It should always be remembered that physical exercise definitely improves the carbohydrate metabolism in suitable cases of diabetes. The value of physical exercise as a prophylactic measure in diabetes is also undoubted in the light of the present-day research.

Avoidance of mental worries—It should be borne in mind that mental worry increases the blood sugar and causes increased sugar excretion in the urine and hence should be avoided as much as possible. An occasional relaxation in the shape of a trip to the hills or other pleasure resorts often helps to bring about a great improvement in the physical condition of the diabetic patient.

Avoidance of overweight—Over weight is very undesirable for diabetic patients and it should be the endeavour of every patient to maintain a normal weight according to his age and height. Joslin's remark that diabetes is a penalty to obesity seems very appropriate.

Avoidance of infections—Infections of any kind definitely lowers the carbohydrate tolerance in a diabetic patient and visibly increases the severity of the disease. Always beware of such infections as carbuncles, gangrene, abscesses, lobar pneumonia, etc. and report to your physician immediately.

Avoidance of oral sepsis—Scrupulous care of the teeth and the oral hygiene is essential for diabetic patients. The ill effects of pyorrhœa and the absorption of pus therefrom certainly retard the progress of the treatment and may sometimes produce a dangerous condition in diabetic patients.

Avoidance of skin infections—Diabetics should take great care of their skin. They should keep it scrupulously clean and should be very careful of cuts and bruises however simple they may be.

Avoidance of constipation—Diabetics must particularly avoid constipation. If the vegetables in the diet and abdominal exercises fail to bring about normal bowel action, he should resort to mild laxatives but avoid drastic purgatives.

B
AVERAGE WEIGHT OF Males ACCORDING TO AGE AND HEIGHT

HEIGHT	5 0"	5 1"	5 2"	5 3"	5 4"	5 5"	5 6"	5 7"	5 8"	5 9"	5 10"	5 11"	6 0"	6 1"	6 2"	6 3"	6 4"
Age	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94
5 0"	7 9	7 11	8 0	8 3	8 6	8 10	9 0	9 4	9 8	9 12	10 2	10 7	10 12	11 3	11 8	11 13	12 4
5 1"	7 13	8 1	8 4	8 7	8 10	9 0	9 4	9 8	9 12	10 2	10 6	10 11	11 4	11 7	11 12	12 3	12 8
5 2"	8 3	8 5	8 8	8 11	9 0	9 4	9 8	9 12	10 2	10 6	10 10	11 1	11 6	11 11	12 2	12 7	13 12
5 3"	8 6	8 8	8 11	9 0	9 4	9 8	9 12	10 1	10 5	10 9	10 13	11 0	11 8	11 13	12 4	12 9	13 0
5 4"	8 8	8 10	8 13	9 2	9 6	9 10	10 0	10 3	10 7	10 11	11 1	11 5	11 10	12 1	12 7	12 12	13 3
5 5"	8 10	8 12	9 0	9 3	9 7	9 11	10 1	10 5	10 9	10 13	11 3	11 8	11 13	12 3	12 11	13 2	13 7
5 6"	8 13	9 1	9 3	9 6	9 9	9 13	10 3	10 7	10 11	11 1	11 5	11 10	12 2	12 6	13 0	13 6	13 11
5 7"	9 1	9 3	9 5	9 8	9 11	10 1	10 5	10 9	10 13	11 3	11 5	11 13	12 3	12 11	13 3	13 9	14 1
5 8"	9 2	9 4	9 6	9 9	9 12	10 2	10 6	10 10	11 1	11 6	11 11	12 2	12 3	13 0	13 6	13 12	14 4
5 9"	9 3	9 5	9 7	9 10	10 0	10 4	10 8	10 12	11 2	11 8	11 13	12 4	12 10	13 2	13 9	14 1	14 7
5 10"	9 5	9 7	9 9	9 12	10 1	10 5	10 9	10 13	11 4	11 9	12 0	12 6	12 12	13 4	13 11	14 4	14 10
5 11"	9 6	9 8	9 10	9 13	10 2	10 6	10 10	11 0	11 5	11 10	12 1	12 7	12 13	13 5	13 12	14 5	14 12
6 0"	9 8	9 10	9 12	10 1	10 4	10 8	10 12	11 2	11 7	11 12	12 3	12 9	13 1	13 7	14 0	14 7	15 0
6 1"	8	9 10	9 12	10 1	10 4	10 8	10 12	11 2	11 7	11 12	12 3	12 9	13 1	13 8	14 1	14 8	15 1

AVERAGE WEIGHT OF Females According to Age and Height

HEIGHT	4' 8"	4' 9"	4' 10"	4' 11"	5' 0"	5' 1"	5' 2"	5' 3"	5' 4"	5' 5"	5' 6"	5' 7"	5' 8"	5' 9"	5' 10"	5' 11"	6' 0"
AGES	Lb	St Lb	St Lb	St Lb	Lb	St Lb	Lb	Lb	St Lb	Lb	St Lb	St Lb	Lb	St Lb	St Lb	St Lb	St Lb
15-16	7 3	7 5	7 7	7 8	7 9	7 11	8 0	8 3	8 6	8 8	9 0	9 4	9 8	9 12	10 2	10 7	10 12
17-18	7 5	7 7	7 9	7 11	7 13	8 1	8 4	8 7	8 10	8 13	9 3	9 7	9 11	10 0	10 4	10 9	11 0
19-20	7 7	7 9	7 11	7 13	8 1	8 3	8 6	8 9	8 12	9 1	9 5	9 7	9 13	10 2	10 6	10 11	11 1
21-22	7 9	7 11	7 13	8 1	8 3	8 5	8 6	8 11	9 0	9 3	9 7	9 11	10 1	10 4	10 8	10 12	11 2
23-24	7 10	7 12	8 0	8 2	8 4	8 6	8 9	8 12	9 1	9 4	9 8	9 12	10 2	10 6	10 10	10 13	11 3
25-27	7 11	7 13	8 1	8 3	8 5	8 7	8 9	8 12	9 2	9 5	9 9	9 13	10 3	10 7	10 11	11 0	11 4
28-30	7 13	8 1	8 3	8 5	8 7	8 9	8 11	9 0	9 4	9 7	9 11	10 1	10 5	10 9	10 13	11 2	11 6
31-33	8 1	8 3	8 5	8 7	8 9	8 11	8 13	9 2	9 6	9 9	9 13	10 3	10 7	10 11	11 0	11 3	11 7
34-36	8 3	8 5	8 7	8 9	8 11	8 13	9 1	9 4	9 8	9 12	10 2	10 6	10 10	11 0	11 3	11 6	11 9
37-39	8 4	8 6	8 8	8 10	8 12	9 0	9 3	9 6	9 10	10 0	10 4	10 8	10 12	11 2	11 5	11 8	11 11
40-42	8 7	8 9	8 11	8 13	9 1	9 3	9 6	9 9	9 12	10 2	10 6	10 10	11 0	11 4	11 7	11 10	11 13
43-45	8 9	8 11	8 13	9 1	9 3	9 5	9 8	9 11	10 0	10 4	10 8	10 12	11 2	11 6	11 9	11 13	12 2
46-49	8 11	8 13	9 1	9 3	9 5	9 7	9 10	9 13	10 1	10 6	10 10	11 0	11 4	11 8	11 11	12 1	12 4
50	8 13	9 1	9 3	9 5	9 7	9 9	9 12	10 1	10 4	10 8	10 12	11 2	11 7	11 11	12 1	12 5	12 8

C

A FEW USEFUL RECIPES FOR DIABETIC PATIENTS

Broths and soups

Broths and soups are very useful for diabetic patients because their food values are comparatively small while their bulk is fairly large and thus they are *filling to the stomach and satisfying to the appetite*

Clear soups may be made in the ordinary way from stock. Thick soups can be made with stock or water as a basis and various kinds of vegetables may be added to it which will thus give it substance and make it palatable without much increase in the food values. Vegetables such as chopped cabbages, celery, string beans, onions, etc. may be used.

(1) *Clear soup*

Brown stock	8 oz
Onions	2
Celery	2 sticks
White of 2 eggs	
Seasonings	

Remove fat from stock and put into a clean pan. Add the vegetables cut up in thin slices. Beat white of eggs to a stiff froth and add. Bring the mixture to boil slowly whisking occasionally while boiling. Simmer for 10 minutes and strain through muslin. Add salt and seasonings and reboil before serving.

Food values—C=7 P=8 F=negligible

(2) *Tomato soup*

Stock
Tomato
Cream
Onion

Cut the tomatoes in pieces and cook it in stock until quite soft, then rub through a fine sieve rejecting the seeds and skin. Add seasonings and bring it to boil. Add cream just before serving.

Food values— $C=10$, $P=2$, $F=4$

SAUCE AND MAYONNAISE DRESSINGS

(3) Cheese sauce

Yolk of one egg	
Butter	$\frac{1}{2}$ oz
Grated cheddar cheese	$\frac{1}{2}$
Seasonings	

Beat up the yolk of the egg thoroughly, add seasonings and cheese. Melt butter in a sauce pan and put the mixture in it bringing it to boil slowly, stirring all the time.

Food values— $C=0$, $P=8$, $F=25$

(4) Cream sauce

Butter	1 level teaspoonful
Flour	1 " "
Cream	1 oz
Water	1 "
Salt	

Melt the butter add flour and salt and mix until perfectly smooth. Add cream and water and cook for a few minutes.

Food values— $C=3$, $P=1$, $F=15$

(5) Diabetic mayonnaise

Egg	1
Mustard	$1\frac{1}{2}$ teaspoonfuls
Salt	
Saccharine	$\frac{1}{2}$ grain
Mineral oil	8 to 10 oz
Lemon juice	

Beat egg thoroughly. Add the dry ingredients gradually, beat well and add lemon juice. Add mineral oil slowly drop by drop beating constantly. Thin with lemon juice or white vinegar.

Food values—A small quantity of this dressing has practically no food value.

(6) *French dressing*

White vinegar	1 tablespoonful
Olive oil	1 "
Salt and pepper	

Mix ingredients and stir until thoroughly mixed.

Food values—C=0 P=0 F=15

CUSTARD PLDINGS

(7) *Baked custard*

Egg	1
Milk	4 or
Saccharine	

Beat egg well and add milk sweetened with saccharine, a little at a time. Pour the mixture into a dish and bake in a moderate oven for about 15 to 20 minutes.

Food values—C=5 P=9 F=9

(8) *Almond custard*

Milk	3½ oz
Yolk of one egg	
Ground almonds	½ oz
Cinnamon	
Saccharine	
Lemon rind	

Boil the milk with cinnamon and some pieces of lemon rinds for about 5 minutes. Strain and when it cools down

Cut the tomatoes in
quite soft, then rub thro
and skin Add seasonin
just before serving

Food value

SALCI AND

Yolk of on
Butter
Grated h
Seasonin

Beat up the
and cheese Mel
in it bringin-

1

1

1

1

1

5

Melt the
perfectly smol
minutes

Food

(5) 1

Egg
Mustard
Salt
Saccharine
Mineral oil
Lemon juice

(11) *Chhana chapatis* *

Wheat flour	2 oz †
Chhana (dry)	2
Ghee	3 teaspoonfuls
Salt	(to taste)

Mix chhana with flour well together preferably with the hand. Add ghee and mix thoroughly again. Add water gradually and make into a firm dough. Divide into 3 or 4 pieces and put it on a well floured rolling board and roll it evenly.

Bake on an oven and make Chapatis in the usual way.

Food values—C=42 P=18 F=15

* This is recommended for the vegetarian diabetics and is sometimes found to be useful in supplementing protein to their diet in a more palatable form.

† Reserve a spoonful of flour for use on the rolling board for smooth rolling.

to some extent add to it the beaten egg yolk ground almonds and saccharine. Pour it in a cup and stand it in a sauce pan of hot water. Stand the sauce pan over low gas until the mixture begins to thicken. Stir all the time.

Food values—C=7 P=7, F=13

ICE CREAMS

(9) *Chocolate ice cream*

Cocoa	1 teaspoonful
Cream	2 oz
Water	2
Saccharine	$\frac{1}{2}$ gram
Vanilla	$\frac{1}{2}$ teaspoonful

Cook the cocoa in water cool and add cream saccharine and flavourings. Freeze.

Food values—C=4 P=2 F=10

(10) *Diabetic marmalade*

Peel of orange	One (large)
Lemon (large)	One
Saccharine	4 grams
Water	6 ounces
Gelatine leaf	$\frac{1}{4}$ ounce

Peel one large orange wash the skin thoroughly and cut in very small pieces. Peel the lemon and cut the skin in the same way. Mix and chop the two together finely. Add the juice of the lemon and the water. Bring it to a boiling point and simmer for an hour or more adding water whenever necessary to replenish the water lost through boiling. Cut gelatine into strips and add it along with the saccharine. Stir for 10 minutes and put it in a jar to set.

This is practically of no food value

APPENDIX II

A

Approximate amount (in grammes of carbohydrate Protein, Fat and Calories yielded by one ounce (approximately $\frac{1}{2}$ chittack) of common food stuffs

Food values (gms per oz)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Cereal Products				
Arrowroot	25.0	0.1		100
Bajri	19.4	3.2	1.5	109
Barley (raw)	20.6	3.0	0.3	99
(Pearl)	22.0	2.1	0.3	101
Bread (white)	16.0	2.3	0.2	75
(white toasted)	20.0	2.7	0.3	89
(brown)	15.2	2.4	0.4	70
Cambu	19.4	3.6	1.3	105
Chira (beaten rice)	22.1	1.9	0.4	109
Cornflour	26.2	0.1	0.2	101
Khor (fried paddy)	21.0	2.1	traces	100
Muscovoni (raw)	22.1	3.5	0.4	102
Maze tender (bhutta kaucha)	4.2	1.2	traces	25
(Makhi dry)	18.7	3.1	1.0	102
Makhna	21.8	2.7	traces	101
Muri (puffed rice)	20.4	1.8	0.3	90
Oatmeal (raw)	19.0	3.4	1.5	115
= (porridge)	2.3	0.4	0.3	13
(Scotch)	20.1	3.6	1.8	112
Oats, rolled (quaker)	18.8	4.5	2.1	115

D

TABLE OF APPROXIMATE EQUIVALENTS

Household fluid measures

- 1 teaspoonful corresponds to $\frac{1}{2}$ oz or 3.5 c.c.
- 1 dessertspoonful corresponds to $\frac{1}{2}$ oz or 7 c.c.
- 1 tablespoonful corresponds to $\frac{1}{2}$ oz or 15 c.c.
- 1 egg cupful corresponds to 1 oz or 30 c.c.* or $\frac{1}{2}$ chittack
- 1 wine glassful corresponds to 2 oz or 1 chittack
- 1 teacupful corresponds to 6 oz or 3 chittacks
- 1 tumblerful corresponds to 8 oz or 1 *poa*

Imperial weights and measures

- 1 fluid oz corresponds to 30 c.c.*
- 1 fluid oz ($1\frac{1}{2}$ pints) correspond to 1,000 c.c. (1 litre) or 1 seer and $1\frac{1}{2}$ chittacks
- 160 fluid oz (8 pints or 1 gallon) correspond to 4½ litres or 5 seers
- 1 oz corresponds to 30 gm † or $2\frac{1}{2}$ tolas (1 tola = 2 oz)
- 2 oz correspond to 1 chittack (5 tolas)
- 1 pound corresponds to 450 gm or $\frac{1}{2}$ seer (1 seer = 928 gm)
- $2\frac{1}{2}$ lb (35 oz) correspond to 1,000 gm (1 kilo) or 1 seer $2\frac{1}{2}$ chittacks
- 1 stone (14 lb) corresponds to 6½ kilos or 6½ seers

Conversion factors

- To convert ounces into grammes multiply by 28.35
- To convert pounds into kilogrammes multiply by 0.453
- To convert grammes into ounces multiply by 0.035
- 1 silver rupee weighs 1 tola or 11.36 gm or $\frac{1}{2}$ oz approximately
- 1 four anna bit weighs 2.84 gm or $1/10$ oz approximately
- 1 Indian bazaar seer weighs 80 tolas or 928 gm or $32\frac{1}{2}$ oz approximately

Caloric value of food stuffs

- 1 gramme of carbohydrate yields 4.1 calories
- 1 gramme of protein yields 4.1 calories
- 1 gramme of fat yields 9.3 calories
- 1 c.c. of alcohol yields 5.6 calories

* Actually 28.35 c.c.

† Actually 28.35 gm

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Prote in	Fat	Calor e
Cereal Products—contd				
Force	38	7.6	0.5	105
Groundnuts	14	34	0.9	107
Ground wheat	27.4	7.8	0.8	103
Lentils (dry)				
Besan (powdered chnl)	16.5	6.4	0.9	102
Labli (cow gram)	15.8	7.0	0.7	101
Dal average)	15.9	6	0	100
(dhal) red gram	16.2	6.3	0.5	104
(chola) Bengal	17.0	4.9	1.5	117
(channa)	16.5	8.0	0.7	10
(kitcha)	15.8	6.3	0.4	111
(matar)	16.1	5.6	0.3	96
(Mussor)	16.9	7.1	0.7	105
(moong)	16.0	6.8	0.4	107
Grounded (bajra chola)	16.8	6.4	1.5	119
whole (chola)	17.3	4.8	1.5	109
Harot beans	17.9	6.1	trace	3
Masoor Kabli (dry peas)	16.0	6.0	trace	96
Soya bean (flour)	4.0	11.5	0	173
Sallap (powdered gram)	17.1	7.6	0.6	107
Milk and Milk Products				
Butter (fresh)	0.0	0.1	24.0	218
Butter milk (gf l) unsweetened	0.4	0.8	trace	88
Chhanda (fresh milk curd)	0.1	6.0	5.0	—

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Cereal Products—contd				
Rice (average)	24.5	1.4	0.2	104
„ beaten (<i>chira</i>)	22.1	1.9	0.4	106
„ boiled (<i>bhat</i>)	10.4	0.6	traces	45
„ fried paddy (<i>khoi</i>)	21.0	2.1	traces	100
„ Old (<i>dadghani</i>)	24.0	1.5	traces	108
„ parboiled home pounded (<i>siddha</i>)	22.0	2.4	traces	106
„ puffed (<i>muri</i>)	20.4	1.8	0.3	90
„ raw home-pounded (<i>atala</i>)	22.2	2.4	traces	102
„ raw milled	22.5	2.0	0.2	102
Rusk (plain unsweetened)	18.7	4.5	2.5	116
Sago	26.7	0.1	traces	101
Sooji (semolina)	15.0	4.2	0.6	80
Tapioca	27.0	0.2	traces	102
Vermicelli	21.0	3.0	0.5	100
Wheat flour refined (<i>maida</i>)	21.5	2.6	0.3	103
Wheat flour (<i>atta</i>)	20.8	3.3	0.5	102
Whole wheat (<i>gehru</i>)	20.1	3.3	0.5	102
Wheat gluten	0.4	6.3	traces	28
Biscuit (average)	21.0	2.1	3.8	120
„ (cream cracker)	16.3	2.4	9.4	138
„ (digestive)	18.7	2.7	5.8	137
Biscuit (sweet mixed)	18.9	1.6	8.7	158
„ (vita weat)	22.1	2.4	2.9	120
„ (water)	20.7	3.0	3.5	126
Barley	16.2	2.3	1.7	87

APPENDIX II (A)—(continued)

Food stuffs	Carbo hydrate	Protein	Fat	Calories
Green Vegetables				
Green vegetables (average)	14	02	traces	5
Asparagus (<i>soot mooler</i>)	07	07	traces	6
Beans, broad (<i>seem</i>)	28	13	traces	17
Beans string (<i>barbat</i>)	17	07	traces	11
Letel leaves (<i>pan</i>)	17	09	traces	13
Brinjal (<i>daigun</i>)	18	04	traces	10
Brussels sprouts (<i>choiz banda kabi</i>)	12	06	traces	15
Cabbage (<i>banda kabi</i>)	14	03	traces	9
Cauliflower (<i>phool kabi</i>)	08	05	traces	9
Celery (<i>shalarri</i>)	15	05	traces	9
Cucumber (<i>khira soshu</i>)	08	traces	traces	4
Drum stick (<i>sajins datu</i>)	08	07	traces	9
Endive (<i>kasni leaves</i>)	07	traces	traces	6
French beans	13	05	traces	8
Gourd, Ishi (<i>chhachi kumra</i>)	09	traces	traces	5
, bitter, large (<i>karela</i>)	12	05	traces	11
, bitter small (<i>ucchay</i>)	27	traces	traces	18
, bottle (<i>ian kaddu</i>)	08	traces	traces	4
, club (<i>dhundul</i>)	10	02	traces	5
, Sponge (<i>fhinga</i>)	04	traces	traces	
, snake (<i>chichinga</i>)	10	01	traces	5
, white (<i>chaul kumra</i>)	09	traces	traces	4
Jack fruit unripe (<i>inchar</i>)	27	07	traces	15
seeds (<i>kantabij dry</i>)	109	19	traces	53
Lady's finger (<i>dhanash bhunder</i>)	20	06	traces	12

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Milk and Milk Products—contd				
Cheese (American)	0.3	8.1	10.1	128
„ (Cheddar)	traces	7.1	9.6	119
„ (Dutch)	traces	8.0	4.8	77
„ (cream)	traces	0.9	24.5	232
„ (Gorgonzola)	traces	7.1	8.8	112
„ (Gruyère)	traces	10.4	9.5	131
Curds (<i>Dahi</i>) unsweetened	0.9	0.8	0.8	16
Ghee (Clarified butter)	0.0	0.0	25.0	228
Milk (ass)	1.7	0.7	0.5	15
„ (buffalo)	1.5	1.2	2.5	28
„ (cow)	1.4	0.9	1.1	19
„ (skimmed)	1.4	1.0	traces	11
„ (Goat)	1.4	1.1	1.1	20
„ (human)	2.0	0.3	1.0	18
„ (sheep)	1.8	0.6	traces	13
„ powder (whole)	10.0	7.3	8.0	146
„ powder (skim)	14.5	10.8	traces	104
„ powder ('Lhm')	11.0	7.6	7.6	
„ powder (Horlicks)	19.0	4.5	2.6	114
„ malted (average)	21.3	3.6	2.0	121
„ malted (Horlick)	20.1	4.1	2.4	114
Milk condensed, whole (unsweetened)	3.5	2.2	2.4	44
„ condensed, whole (sweetened)	15.9	2.3	3.4	100
„ Khos (<i>khos khos</i>)	5.8	4.1	8.8	124
„ Whey	1.4	0.2	traces	8

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calorie
Tubers and Root Vegetables				
Artichoke (<i>kathichuk</i>)	45	10	traces	23
Peet (<i>chukander</i>)	40	05	traces	18
Carrot (<i>gajar</i>)	25	03	traces	13
Knol Kole (<i>ole kabi</i>)	17	03	traces	8
Leek (<i>bilati phaj</i>)	29	05	traces	14
Mankachu	55	02	04	25
Ole	36	06	08	21
Onion (<i>phaj</i>) big	33	03	traces	16
" " small	38	03	traces	18
Onion stalk (<i>phaj kali</i>)	25	03	traces	12
Parsnips	32	04	traces	14
Pepper Green (<i>kancha lanka</i>)	17	08	traces	12
Potatoes (<i>alu</i>)	55	05	traces	25
" " "Ch ps"	106	11	28	68
" " boiled	53	07	traces	27
" " New	50	05	traces	22
" " Sweet (<i>ranga alu</i>)	88	03	traces	38
Raddish (<i>moola</i>), pink	21	02	traces	10
" " white	12	02	traces	6
Shankalu	62	04	traces	27
Turnip (<i>shalgam</i>)	22	01	traces	10
Yam (<i>kachu</i>)	60	04	traces	23
Fresh Fruits				
Amli (<i>amlaki</i>)	42	01		17
Apples (ordinary)	38	01	traces	15

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Green Vegetables—contd				
Lettuce (<i>saladh</i>)	0.6	0.6	traces	7
Mango, green	2.5	0.2	traces	12
Mint (<i>pudina</i>)	2.2	1.3	traces	11
Mushroom	2.0	1.0	0.1	13
Papaya, green	0.1	0.2	traces	2
Patal (<i>phulal</i>)	0.6	0.5	traces	6
Peas, green (<i>kalai mti</i>)	5.6	2.0	traces	32
Pepper green (<i>kuncha lanka</i>)	1.7	0.8	traces	10
Plantain flower (<i>mocha</i>)	1.4	0.4	traces	8
„ green (<i>kuncha kala</i>)	4.2	0.2	traces	18
„ stem (<i>thor</i>)	2.7	0.1	traces	12
Pumpkin, red (<i>kumra</i>)	2.0	0.3	traces	8
Rhubarb	1.0	0.1	traces	5
Sag (<i>dhanla</i>) coriander leaves	1.9	0.9	0.2	13
„ (<i>kalmsi</i>)	1.2	0.5	traces	8
„ (<i>kochu</i>)	1.2	0.1	traces	6
„ (<i>notay</i>) dwarf spinach	0.9	0.4	traces	6
„ (<i>palong</i>) Indian spinach	1.1	0.6	traces	9
„ (<i>poyses</i>) Malabar night shades	0.3	0.3		
Sag (<i>palta</i>)	0.3	1.4	traces	6
„ (<i>pudina</i>) Mint	2.2	1.3	traces	16
„ (<i>sarsey</i>) Rape plant stem	1.1	0.9	traces	6
Tomato (<i>bilati baigun</i>)	1.2	0.4	traces	7
Vegetable marrow (<i>bilati kumra</i>)	1.1	0.1	traces	■

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Fresh Fruits—continued				
Apple (Himalayan)	20	0.6	traces	8
Apple (Himalayan)	11	traces		5
Orange (Himalayan)	24	0.7	traces	10
Orange juice	27	0.7	trace	11
Alumina fruit (Himalayan)	19	0.1		9
Apple (Himalayan) water cleant	68	1.3	traces	34
Apple (Himalayan)	27	0.1	traces	12
Apple (Himalayan)	35	0.7	traces	15
Apples (fresh)	26	0.2	traces	11
Apple (Himalayan)	33	0.1	trace	14
Apple (Himalayan)	30	0.1	traces	11
Apple (Himalayan)	37	0.1	trace	14
Apple (Himalayan)	27	0.7	traces	11
Apple (Himalayan)	21	0.7	traces	10
Apple (Himalayan)	66	0.7		4
Apple (Himalayan)	33	0.1	trace	13
Apple (Himalayan)	29	0	traces	13
Apple (Himalayan)	14	0.4	traces	7
Apple (Himalayan)	18	0.7	traces	7
Apple (Himalayan)	66	0.4	traces	27
Apple (Himalayan)	88	0.4	traces	37
Apple (Himalayan)	17	0.4	traces	7
Dried Fruits				
Apple (Himalayan)	173	1.6	traces	52
Apple (Himalayan)	191	0.6	traces	0

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calor
Fresh Fruits—contd				
Banana (singapuri)	61	0.3		2
.. (chatim kela)	50	0.3		20
.. (champa kela)	42	0.3		16
Bael	45	0.2	traces	21
.. (kajel) wood apple	43	2.0	traces	28
Blackberry (kaijam)	10	0.4	traces	8
Bullock's heart (amra)	59	0.4	traces	26
Coco nut water (dab pani)	0.7	0.4		5
.. Kernel (narkel)	39	1.7	15.1	134
Cucumber (sasha khira)	0.5	traces	traces	3
Figs	48	0.4	traces	12
Gooseberry (lepani)	33	0.3		15
Grapes (white) Angoor	46	0.2	traces	18
.. (black variety)	44	0.2	traces	17
Grape fruit	15	0.2	traces	6
Gruva (peara Deshi)	20	0.2	traces	12
.. (Kashu)	33	0.3	traces	15
Jack fruit (kantai)	55	0.4	traces	25
Lemon (pat nambu)	23	0.2	traces	12
Lichee (lichu)	20	0.8	traces	11
Lime, sweet (sarbat nebu)	36	0.3	traces	14
Loquat (loket)	15	traces	traces	6
Mango ripe (Deshi)	36	0.2		15
.. (langrah)	51	0.5		24
.. (Bombay)	54	0.5	traces	26
Melon (footee)	14	0.2	traces	6

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Condiments Spices etc—contd				
Mustard (oil)	6.8	6.3	11.3	139
Nutmeg (nutmeg)	8.1	2.1	10.3	133
Onion (Asian)	11.3	4.5	5.4	113
Pepper (black) (whole)	14.1	3.3	1.9	91
Tamarind ripe (Tentul)	8.8	0.4	traces	37
green	2.2	0.4		13
Turnip (whole)	1.8	1.7	1.4	28
Eggs				
Egg duck (whole)	0.0	3.8	3.8	52
(white)	0.0	2.6	traces	11
Egg (whole)	0.0	4.6	8.7	90
hen (whole)	0.0	3.6	3.6	50
Fish				
Crab (muscle)	1.0	2.5	0.3	17
Fish (average)	0.0	5.5	1.0	32
Belah	0.0	4.1	0.1	19
Bhangor	0.0	4.1	2.4	40
Bhetki	0.0	4.2	0.6	25
Herrings (white)	0.0	4.7	4.7	58
Hilsa (Hilsa)	0.0	6.7	5.5	77
Katla	0.0	5.5	0.7	29
Kol	0.0	6.1	0.1	26
Lola	0.0	5.3	0.1	24
Mugur	0.0	5.5	0.2	21
Mungo (topsi)	0.0	4.7	1.2	31

APPENDIX II (A)—(Continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Dried Fruits—contd				
Figs dried (<i>Anjeer</i>)	15.0	1.0	traces	61
Prunes	11.5	0.7	traces	48
Raisins (<i>kismis</i>)	18.3	0.3	traces	70
Nuts				
Almonds (<i>kaju</i> ; <i>badam</i>)	3.0	5.9	15.2	170
Brazil nuts	2.1	5.1	17.3	183
Cashew nuts (<i>kaju</i> <i>badam</i>)	6.3	6.0	13.3	144
Chestnuts	10.4	0.7	0.8	49
Coco-nut kernel	3.9	1.7	15.9	134
Peanut (<i>china</i> <i>badam</i>)	5.7	7.5	11.4	160
" roasted	5.5	9.0	11.3	165
Pistachio nuts (<i>pesta</i>)	4.6	5.6	15.2	153
Walnuts (<i>akhrot</i>)	3.1	4.4	18.3	109
Condiments, Spices, etc				
Asafoetida (<i>hing</i>)	19.2	1.1	0.3	90
Cardamom (<i>alaich</i>)	11.9	2.8	0.6	70
Chillies green (<i>pancha</i> <i>lanka</i>)	1.8	0.8	0.2	12
dry (<i>sukna</i> <i>lanka</i>)	8.9	4.5	1.7	74
Cloves (<i>ladanga</i>)	13.6	1.5	2.5	87
Coriander (<i>dhane</i>)	6.2	4.0	4.6	66
Cumin (<i>jira</i>)	10.3	5.3	4.2	106
Fenugreek seeds (<i>methi</i>)	13.0	7.8	1.5	99
Garlic (<i>rasun</i>)	8.2	1.8	traces	43
Ginger (<i>ada</i>)	3.5	0.7	0.3	20
Mace (<i>jaitri</i>)	14.1	1.8	7.2	131

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Meat—contd				
Duck	0.0	6.2	1.8	42
Pork	0.0	6.0	3.1	53
Sheep's kidney	traces	4.7	1.3	31
" liver	0.5	5.4	2.1	44
Tongue (sheep)	0.0	4.5	5.4	67
Turkey (roast)	0.0	5.1	1.3	34
Animal Fats and Vegetable Oils				
Cocoyam	0.0	0.0	28.0	260
Coconut oil	0.0	0.0	28.2	262
Cod liver oil	0.0	0.0	28.4	264
Fat mutton	0.0	0.4	26.4	230
Finchley oil (Til)	0.0	0.0	29.0	260
Groundnut oil	0.0	0.0	28.0	260
Lard	0.0	0.0	29.4	264
Margarine	0.0	0.0	24.2	226
Musard oil	0.0	0.0	28.2	263
Olve oil	0.0	0.0	29.4	261
Sweets				
Peanut pudding	11.4	1.8	3.2	80
Lun	16.2	2.5	1.7	87
Cherry cake	16.0	1.3	6.8	129
Custard (tomato)	11.0	0.3	traces	43
Glucose	25.8	0.0	0.0	106
Honey (pure)	21.7	traces	traces	82
Ice cream (average)	5.0	1.1	3.8	59

APPENDIX II (A)—(Continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Fish—contd				
Fish Mourala	00	51	11	32
„ Mrigali	00	55	01	24
„ Prawn (chingree)	00	54	04	26
„ Parsheli	00	47	18	35
„ Puti	00	51	07	27
„ Rui	00	47	04	23
„ Salmon (salter)	00	57	31	53
„ Singhi	00	65	01	28
„ Sois	00	45	07	25
„ Tangrahi	00	54	13	30
Meat				
Meat butcher's (average)	00	61	30	53
Bacon	00	36	140	144
Beef (corned)	00	64	43	66
„ steak raw	00	55	30	50
Brain	00	29	27	37
Chicken	00	60	14	43
Crab Muscle (kankrahi)	10	25	03	17
Duck	00	51	29	51
Fowl	00	55	46	70
Grat meat	00	71	10	36
Ham (medium fat)	00	43	108	118
Mutton (fat)	00	40	95	105
„ (lean)	00	53	20	42
„ (roasted)	00	71	56	83

APPENDIX II (A)—(continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Miscellaneous—contd.				
Hotels Valted Milk	20.1	4.1	2.4	114
Lebanese extract of beef	0.0	8.6		30
Nestle's (Home made)	1.5	1.3	1.2	23
Marmite	0.0	2.8	traces	12
Mellin's food	22	3.2	0.1	107
Milk line	17.4	3.7	2.2	101
Raw meat juice	0.0	0.5		2
Milk & chicken	9.1	3.5	1.3	64
ham	10.8	2.9	4.0	111
Milk	6.9	1.3	3.6	102
Sup Chicken	0.6	2.9	0.2	16
clear	0.0	1.0	traces	5
pea	3.1	1.4	1.9	36
toasted	1.5	0.4	0.3	11

APPENDIX II (A)—(Continued)

Food stuffs	Carbo- hydrate	Protein	Fat	Calories
Sweets—<i>cond</i>				
Jaggery	27.0	0.1	traces	111
Jam	19.7	traces	traces	74
Jam tarts	18.3	1.7	5.6	128
Marmalade	19.8	traces	0.4	74
Mince pies	12.2	1.3	5.6	103
Oat meal biscuit	17.7	2.5	6.8	143
Pastry (cream)	16.4	0.4	3.2	91
Sandesh (best quality)	11.4	5.1	5.6	120
Scones (with egg)	17.0	2.4	3.0	102
Sugar (brown)	26.8	traces	traces	109
Sugar (white)	28.1	traces	traces	112
Treacle (<i>goor</i>)	25.0	traces	traces	100
Cooked Foods				
Boiled rice (<i>bhat</i>)	10.4	0.6	0.1	45
Chapati	19.6	2.6	1.0	100
Loochi (fried in ghee)	14.2	2.1	6.4	130
Parathas (cooked in ghee)	14.2	2.3	5.0	115
Miscellaneous				
Benger's food (dry)	22.8	3.4	traces	107
Blancmange	5.3	0.9	1.1	34
Bourn vita	19.2	3.2	2.1	105
Bouillon	0.0	0.2	traces	1
Evril	0.0	8.3	0.2	36
Cocoa (dry)	10.6	5.1	7.5	134
Cocoa (powder)	9.9	5.8	6.6	128

APPENDIX II (A)—(concluded)

	Carbo- hydrate content	Calories
MINERALS		
Ginger ale (sweet) Schweppes per large bottle 11 oz	26	107
Ginger ale dry per large bottle 11 oz	20	82
Ginger beer per large bottle 16 oz	24	98
Lemonade per bottle 6½ oz	20	78

*Classified list of green and root vegetables (arranged
according to carbohydrate content)*

Class I

Carbohydrate content per ounce—about 1 gramme or
less (equivalent to ¼ teaspoonful of sugar or less)

Asparagus (soot moolte)	Gourd white (chaul kumra)
Caul flower (phool kabi)	Lettuce (saladhi)
Cucumber (sotha kila)	Lapiva green
Drum Stick (safna dala)	Palat (palat)
Endive (karni leaves)	Rhubarb
Gourd Ash (chhacha kumra)	Spinach (palong sag)
Gourd bottle (lau kaddu)	Sag (palla)
Gourd club (dhundhal)	Sag poyee (Malabar night shades)
Gourd snake (chichinga)	Sag notay (dwarf spinach)
Gourd sponge (fhinga)	

Class II

Carbohydrate content per ounce—about 2 grammes
(equivalent to about ½ teaspoonful of sugar)

Beet leaves (pan)	Knolkole (olekobi)
Beans string (barbati)	Leper green (kancha lanka)
Beetroot (baigun)	Lilium flower (mocha)
Brussels sprouts (chola banda kabi)	Pumpkin reel (kumra)
Cabbage (banda kabi)	Radish white & pink (moola)
Celery (shalara)	Sag (dhan)
French beans	Sag (kalmi)
Gourd bitter (large karela)	Sag (kochu)
Leaves finger (dhanrose, dhindec)	Sag (sarset)
	Tomato (bilati baigun)

APPENDIX II (A)—(continued)

Table of Alcoholic Beverages

Alcoholic beverages	Carbo- hydrate (grammes per oz.)	Calories (per oz.)	Alcohol content (c.c. per oz.)
BEERS			
Ale	16	17.0	14
Beer	15	15.0	15
Stout	21	21.0	21
LIQUERS			
Absinthe	traces	79.0	14.2
Benedictine	9.3	109.0	12.8
Crème de menthe	7.9	108.0	13.6
Kummel	9.0	87.0	9.0
Vernouth	2.7	35.0	4.2
SPIRITS			
Brandy	0.0	71.0	12.7
Gin	0.0	48.0	8.5
Rum	0.0	68.0	12.2
Whisky	0.0	40.0	7.1
Bordeaux-claret	traces	14.0	2.5
Burgundy (average)	traces	17.0	3.1
Champagne (dry)	0.5	21.0	3.4
Claret (Italian)	0.0	17.7	3.1
Hock	0.0	12.0	2.2
Madeira	0.5	26.0	4.2
Marsala	1.0	31.6	4.8
Port	1.9	37.0	4.8
Sherry (dry)	0.5	29.0	4.8
„ (sweet)	1.0	31.0	4.8

APPENDIX II (A)—(concluded)

	Carbo- hydrate content	Calories
MINERALS		
Cherry ale (sweet) Schneppes per large bottle 11 oz	6	10
Ginger beer per large bottle 11 oz	70	82
Ginger beer per large bottle 16 oz	24	38
Lemonade per bottle 6 1/2 oz	20	78

*Classified list of green and root vegetables (arranged
according to carbohydrate content)*

Class I

Carbohydrate content per ounce—about 1 gramme or
less (equivalent to 1/3 teaspoonful of sugar or less)

Asparagus (sool + ooltee)	Go rd white (chaul kunra)
Cauliflower (phool koh)	Lettuce (aladh)
Cucumber (soshu khra)	Lapsa green
Drumstick (saj + dhat)	Patol (palal)
Enive (kas + leetes)	Rhahar
Gourli Ash (chhac + khar)	Spinach (palong sag)
Gourd bottle (la kaddu)	Sag (palla)
Gourd elai (lu dhal)	Sag poyee (Malabar night shade)
Gourd snake (eli + nga)	Sag nolay (dwarf spinach)
Gourd sprig (laga)	

Class II

Carbohydrate content per ounce—about 2 grammes
(equivalent to about 1/2 teaspoonful of sugar)

Betel leaves (pa)	Khol khol (olekoda)
Bean string (barba)	L per green (ka cha lanka)
Bhujal (bhagun)	Plantain illiwer (mocha)
Brussels sprouts (clota banda koti)	Pumpkin reel (kumra)
Calhove (banda kodi)	Rail hili te + pink (moola)
Celery (shajam)	Sag (dhane)
Green bean	Sag (kaim)
Gourd bitter (large kare)	Sag (korhu)
Lily finger (dhanose bhildee)	Sag (sare)
	Tomato (bhil badgun)

Class III

Carbohydrate content per ounce—about 3 grammes
(equivalent to about $\frac{3}{4}$ teaspoonful of sugar)

Beans broad (*seem*)
Carrot (*gajar*)
Gourd small (*ucchay*)
Jack fruit unripe (*inchar*)
Leeks (*bilati piaf*)

Mango green
Onion stalk (*piaf kali*)
Mint Sag (*judina*)
Plantain stem (*thor*)
Turnip (*shalgam*)

Class IV

Carbohydrate content per ounce—about 4 grammes
(equivalent to about 1 teaspoonful of sugar)

Beet (*chukander*)
Ole

Onion large and small
Parsnips

Class V

Carbohydrate content per ounce—about 5 grammes
(equivalent to about $1\frac{1}{4}$ teaspoonful of sugar)

Artichoke (*hathichuk*)

Plantain green (*ka ich kola*)

Class VI

Carbohydrate content per ounce—about 6 grammes
(equivalent to about $1\frac{1}{2}$ teaspoonfuls of sugar)

Lam (*kachu*)
Wankachu

Peas green (*kalai suli*)
Potatoes

*Classified list of fruits (arranged according to
carbohydrate content)*

Class I

Carbohydrate content per ounce—about 1 gramme
(equivalent to about $\frac{1}{4}$ teaspoonful of sugar)

Blackberry (*kalajari*)
Coco-nut water (*dab pani*)

Cucumber (*sosha khira*)
Water melon (*turbuf*)

Pomegranates (*dahim*)

Class II

Carbohydrate content per ounce—about 2 grammes
(equivalent to about $\frac{1}{2}$ teaspoonful of sugar)

Grap fruit	Mu k nelo kla b ja)
Gua a (pea a des)	I al n ra f u t Tal i a
L cle e (l cl)	Plu n red ar ct koo
Loquet (oket)	■ che r go abja
Mel n (foo ee)	Stri berr

Class III

Carbohydrate content per ounce—about 3 grammes
(equivalent to about $\frac{3}{4}$ teaspoonful of sugar)

Le non (pall eb)	P neapple a a a
Papaya (or i nar)	Plu n k o
P tel e	I umelo bat ab eb)

Class II

Carbohydrate content per ounce—about 4 grammes
(equivalent to about 1 teaspoonful of sugar)

Apple (ord nar)	L e (sa ball e eb)
Coconut kernel (arket)	M nio (he l)
Cherry (lepa l)	P pa a he t Rancel
G a a (pea a ka)	Pear naspat)
Lo egranates (be ta a	

Class I

Carbohydrate content per ounce—about 5 grammes
(equivalent to about $1\frac{1}{2}$ teaspoonful of sugar)

An la (a lok)	I s
B el	Gripe w i e t e)
Bana a (chat kela)	Cr pea l la k r et
■ ana (cl a pa kela)	W n (L a a a an l Don l a)
W uaple (ka et bael	

Class II

Tanana (Si cap ri kela)	J ck fru t ka lal)
Juli ck l cart a a)	Water cle thut panipal)
Sugar-cane	

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